AMARIN CORP PLC\UK Form 424B5 July 08, 2013 Table of Contents

The Information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting offers to buy these securities, in any state or other jurisdiction where the offer or sale is not permitted.

Filed Pursuant to Rule 424(b)(5) File No. 333-173132

### **SUBJECT TO COMPLETION, DATED JULY 8, 2013**

### PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated March 29, 2011)

# 21,700,000 American Depositary Shares

Representing 21,700,000 Ordinary Shares

We are offering 21,700,000 American Depositary Shares, or ADSs. Each ADS represents one of our ordinary shares, par value £0.50 per share. Our ADSs are listed on The NASDAQ Global Market under the symbol AMRN . On July 5, 2013, the last reported sale price of our ADSs on The NASDAQ Global Market was \$5.96 per share.

Investing in our ADSs involves a high degree of risk. Please read <u>Risk Factors</u> beginning on page S-6 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

The underwriters have agreed to purchase the ADSs from us at a price of \$ per share, which will result in \$ net proceeds to us before deducting estimated offering expenses payable by us. The underwriters may offer the ADSs from time to time for sale in one or more transactions on the Nasdaq Global Market, in the over-the-counter market, through negotiated transactions or otherwise at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices. See Underwriting .

The underwriters may exercise their option to purchase up to an additional 3,255,000 ADSs from us, at the price per share set forth above for 30 days after the date of this prospectus supplement. If the underwriters exercise the option in full, we would receive an additional \$\\$ in net proceeds before deducting estimated offering expenses payable by us.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Delivery of the ADSs is expected to be made on or about , 2013.

**Citigroup** Jefferies

Prospectus supplement dated , 2013.

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You should rely only on the information contained in or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement and accompanying prospectus entitled. Where You Can Find More Information and Incorporation of Certain Information by Reference.

#### ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer only to the prospectus, we are referring to both parts combined.

In this prospectus supplement, the Company, we, us, our and similar terms refer to Amarin Corporation plc and its subsidiaries on a consolidate basis. References to our ordinary shares or common shares refer to the ordinary shares of Amarin Corporation plc. References to ADSs refer to American Depositary Shares, each of which represents one ordinary share of Amarin Corporation plc.

All references in this prospectus supplement to our consolidated financial statements include, unless the context indicates otherwise, the related notes.

This prospectus supplement, the accompanying prospectus, and the information incorporated by reference herein and therein includes trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners.

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#### PROSPECTUS SUPPLEMENT SUMMARY

The following summary of our business highlights some of the information contained elsewhere in or incorporated by reference into this prospectus supplement or the accompanying prospectus. Because this is only a summary, however, it does not contain all of the information that may be important to you. You should carefully read this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, which are described under Where You Can Find More Information and Incorporation of Certain Information by Reference in this prospectus supplement and the accompanying prospectus. You should also carefully consider the matters discussed in the section in this prospectus supplement entitled Risk Factors and in the accompanying prospectus and in other periodic reports incorporated by reference herein and therein.

### **Our Company**

We are a biopharmaceutical company with expertise in lipid science focused on the commercialization and development of therapeutics to improve cardiovascular health. On July 26, 2012, we received U.S. Food and Drug Administration, or FDA, approval to market and sell our lead product Vascepa® (icosapent ethyl) capsules (formerly known as AMR 101) as an adjunct to diet to reduce triglyceride levels in adult patients with severe ( $TG \ge 500 \text{mg/dL}$ ) hypertriglyceridemia, which we sometimes refer to as the MARINE indication. Triglycerides are fats in the blood. Vascepa became commercially available in the United States by prescription in January 2013, when we commenced sales and shipments to its network of U.S.-based wholesalers and specialty pharmacy providers. On January 28, 2013, we commenced our full commercial launch of Vascepa in the United States for use in the MARINE indication.

We are also developing Vascepa for the treatment of patients with high triglyceride levels (TG  $\geq$ 200 mg/dL and <500 mg/dL) who are also on statin therapy for elevated LDL-C levels. This indication is referred to as mixed dyslipidemia or the ANCHOR indication. In February 2013, we submitted a supplemental New Drug Application, or sNDA, to the FDA seeking approval of Vascepa for the ANCHOR indication. In April 2013, the FDA notified us that it accepted the sNDA for review. The acceptance of the sNDA indicates that the application is sufficiently complete to permit a substantive review by the FDA. On June 18, 2013, the FDA informed us that it plans to convene an advisory committee in October 2013 to review our sNDA seeking approval for the marketing and sale of Vascepa for the treatment of patients with high triglyceride levels (TG  $\geq$ 200 mg/dL and <500 mg/dL) who are also on statin therapy for elevated LDL-C levels. The application is subject to a standard review and has been assigned a Prescription Drug User Fee Act, or PDUFA, date of December 20, 2013. The PDUFA date is the target date for the FDA to complete its review of the sNDA. However, there can be no assurance that the FDA will complete its review of the sNDA by this date.

We believe that our sales and marketing team is well positioned to support the commercialization of Vascepa for the MARINE indication. Upon approval of the ANCHOR indication, we anticipate that we will need to increase our commercial presence, alone or in conjunction with commercial partners, in order to fully maximize Vascepa s commercial opportunity in this patient population. From time to time we have held discussions with larger pharmaceutical companies on potential collaborations and other strategic opportunities, and we intend to continue having discussions regarding such opportunities in the future. However, we cannot estimate the timing of any such potential strategic transaction, and no assurance can be given that we will enter into any such strategic transaction. Until such time as we enter into such a strategic transaction, if ever, we plan to continue to execute on our plans to market and sell Vascepa on our own.

In December 2011 we announced commencement of patient dosing in our cardiovascular outcomes study of Vascepa, titled REDUCE-IT (Reduction of Cardiovascular Events with EPA — Intervention Trial), which is designed to evaluate the efficacy of Vascepa in reducing major cardiovascular events in a high risk patient

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population on statin therapy. We do not believe the final results of the REDUCE-IT study will be required for FDA approval of Vascepa for the ANCHOR indication, although there can be no assurance that this will be the case.

The potential efficacy and safety of Vascepa was studied in the MARINE trial and the ANCHOR trial, each of which were Phase 3 clinical trials. At a daily dose of 4 grams of Vascepa, the dose at which Vascepa is FDA-approved for the MARINE indication, these trials showed favorable clinical results in their respective patient populations in reducing triglyceride levels without increasing LDL-C levels in the MARINE trial and with a statistically significant decrease in LDL-C levels in the ANCHOR trial, in each case as compared to placebo. These trials also showed favorable results, particularly with the 4-gram dose of Vascepa, in other important lipid and inflammation biomarkers, including apolipoprotein B (apo B), non-high-density lipoprotein cholesterol (non-HDL-C), total-cholesterol (TC), very low-density lipoprotein cholesterol (VLDL-C), lipoprotein-associated phospholipase A2 (Lp-PLA2), and high sensitivity C-reactive protein (hs-CRP). In these trials, the most commonly reported adverse reaction (incidence >2% and greater than placebo) in patients treated with Vascepa was arthralgia (joint pain) (2.3% for Vascepa vs. 1.0% for placebo).

### **Commercialization Update**

Vascepa became commercially available in the United States by prescription in January 2013 when we commenced sales and shipments to our network of U.S.-based wholesalers. On January 28, 2013, we commenced our full commercial launch of Vascepa in the United States. In preparation for our commercial launch, we hired and trained a direct sales force of approximately 275 sales representatives. We also employ various marketing and medical affairs personnel to support our commercialization of Vascepa.

In June 2013, we completed our fifth full calendar month of marketing and selling Vascepa. As of the date hereof, based on monthly compilations of data provided by a third party, the estimated number of normalized total Vascepa prescriptions (TRx) for the first four calendar months were as follows: 3,224 (Feb); 7,260 (Mar); 12,314 (Apr); and 16,076 (May). As of the date hereof, based on weekly compilations of data from a third party source for the four weeks ended June 28th, the estimated number of normalized total Vascepa prescriptions (TRx) for June is 18,367 (partial data available). Data provided for June excludes the last two calendar days of June; weekly compilations generally tend to understate the number of prescriptions in the monthly compilations. Normalized total prescriptions represent the estimated total number of Vascepa prescriptions shipped to patients, calculated on a normalized basis (i.e., total capsules shipped divided by 120 capsules, or one month s supply). The data reported above is based on information made available to the Company from a third party resource and may be subject to adjustment and may overstate or understate actual prescriptions.

As of June 30, 2013, over 7,300 clinicians have written prescriptions for Vascepa.

Although we believe these data are prepared on a period-to-period basis in a manner that is generally consistent and that such results are generally indicative of current prescription trends, these data are based on estimates and should not be relied upon as definitive. In addition, as described in our most recent quarterly report on Form 10-Q, because of our limited selling history, during the quarter ended March 31, 2013, we only recognized revenue on product that we could substantiate being resold by retailers, such as pharmacies, for purposes of fulfilling prescriptions. Those prescription data may differ from the prescription data provided above or otherwise reported by third parties.

Because of our limited selling history, we do not believe that we can provide a reasonably accurate forecast of Vascepa prescriptions or revenues. We provide no guidance regarding anticipated levels of Vascepa prescriptions or revenues and no such guidance should be inferred from the operating metrics described above. We believe that investors should view the above-referenced operating metrics with caution, as data for this limited period may not be representative of a trend consistent with the results presented or otherwise predictive of future results. Seasonal fluctuations in pharmaceutical sales, for example, may affect future prescription trends of Vascepa, as could changes in prescriber sentiment and other factors. We believe investors should consider our results over several quarters, or longer, before making an assessment about potential future performance.

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The commercial launch of a new pharmaceutical product is a complex undertaking, and our ability to effectively and profitably launch Vascepa will depend in part on our ability to generate market demand for Vascepa through education, marketing and sales activities our ability to achieve market acceptance of Vascepa, our ability to generate product revenue and our ability to receive adequate levels of reimbursement from third-party payers. See *Risk Factors Risks Related to the Commercialization and Development of Vascepa*.

### **Corporation Information**

Amarin Corporation plc (formerly Ethical Holdings plc) is a public limited company listed in the United States on the NASDAQ Global Market. Amarin was originally incorporated in England as a private limited company on March 1, 1989 under the Companies Act 1985, and re-registered in England as a public limited company on March 19, 1993. Our registered office is located at One New Change, London EC4M 9AF, England. Our principal executive offices are located at 2 Pembroke House, Upper Pembroke Street 28-32, Dublin 2, Ireland and our telephone number is +353-1-6699-020. Our primary U.S. offices are located at 1430 Route 206, Bedminster, NJ 07921.

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#### THE OFFERING

ADSs offered by us 21,700,000 ADSs

Option 3,255,000 ADSs

Ordinary shares to be outstanding after this offering 172,432,881 shares (175,687,881 shares if the option is exercised in full) Use of proceeds

We intend to use the net proceeds from this offering to continue the commercial launch of Vascepa® (icosapent ethyl) capsules in the MARINE indication, prepare for and commercially launch Vascepa in the ANCHOR indication, if approved, advance our REDUCE-IT cardiovascular outcomes trial, and for general corporate and working capital purposes. See Use of Proceeds.

#### **Risk Factors**

This investment involves a high degree of risk. See the information contained in or incorporated by reference under Risk Factors beginning on page S-6 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

### **NASDAQ Global Market symbol**

#### **AMRN**

The number of ordinary shares to be outstanding after this offering is based on 150,732,881 ordinary shares outstanding on June 30, 2013 and excludes as of that date:

11,284,725 ADSs, each ADS representing one ordinary share, issuable upon exercise of outstanding options, at a weighted average exercise price of \$7.47 per share, issuable under our 2002 Stock Option Plan and 2011 Stock Incentive Plan, or the Plans, and other equity incentive plans;

warrants to purchase a total of 9,866,826 ADSs, each ADS representing one ordinary share, at a weighted average exercise price of \$1.44 per share;

7,240,625 ADSs, each ADS representing one ordinary share, available for grant under our 2011 Stock Incentive Plan; and

ADSs issuable upon the conversion of our outstanding 3.5% exchangeable senior notes due 2032 in the aggregate principal amount of \$150.0 million.

If the underwriters option is exercised in full, we will issue and sell an additional 3,255,000 ADSs and will have 175,687,881 ordinary shares outstanding after the offering.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their option.

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#### RISK FACTORS

An investment in our ADSs and our ordinary shares involves a high degree of risk. Before deciding whether to invest in our ADSs and our ordinary shares, you should consider carefully the risks described below, together with other information in this prospectus supplement, the accompanying prospectus and the information and documents incorporated by reference in this prospectus supplement and the accompanying prospectus, including (i) our most recent quarterly report on Form 10-Q for the quarter ended March 31, 2013 which is on file with the SEC and is incorporated herein by reference and (ii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus supplement. Any of these risks could seriously harm our business, financial condition, results of operations or cash flow, resulting in the decline of the trading price of our ADSs and a loss of all or part of your investment.

### Risks Related to the Commercialization and Development of Vascepa

We are dependent upon the success of Vascepa, which only recently obtained FDA approval and launched commercially in the MARINE indication.

As a result of our reliance on a single product and our primary focus on the U.S. market in the near-term, much of our near-term results and value as a company depends on our ability to execute our commercial strategy for Vascepa in the United States, which we only recently launched in January 2013. If commercialization efforts for Vascepa in the MARINE indication or, if approved, the ANCHOR indication, are not successful, our business will be materially and adversely affected. Even if we are able to develop additional products from our research and development efforts, the development time cycle for products typically takes several years. This restricts our ability to respond to adverse business conditions for Vascepa. If we are not successful in developing any future product or products, or if there is not adequate demand for Vascepa or the market for such product develops less rapidly than we anticipate, we may not have the ability to effectively shift our resources to the development of alternative products or do so in a timely manner without suffering material adverse effects on our business. As a result, the lack of alternative products we develop could constrain our ability to generate revenues and achieve profitability.

We recently launched Vascepa in the MARINE indication in the United States with our own, newly established sales and marketing teams and distribution channels and we may not be successful. Historical results may not be consistent with or predictive of future results.

In late January 2013, we began selling and marketing Vascepa in the United States through our own, newly established sales and marketing teams and through a newly established third-party commercial distribution infrastructure. We hired key personnel in these areas over the last several years and hired and trained a professional sales force in early January 2013. The commercial launch of a new pharmaceutical product is a complex undertaking for a company to manage, and we have very limited experience as a company operating in this area. Factors related to building and managing our own sales and marketing organization that can inhibit our efforts to successfully commercialize Vascepa on our own include:

our inability to attract and retain adequate numbers of effective sales and marketing personnel;

our inability to adequately train our sales and marketing personnel, in particular as it relates to various healthcare regulatory requirements applicable to the marketing and sale of pharmaceutical products, and our inability to adequately monitor compliance with these requirements;

the inability of our new sales personnel, working for us as a new market entrant, to obtain access to or persuade adequate numbers of physicians to prescribe Vascepa;

the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and

unforeseen costs and expenses associated with operating a new independent sales and marketing organization.

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In addition, we believe that investors should view with caution both the results for the first quarter of 2013 and as-reported monthly Vascepa prescription numbers for February through June of 2013, as data for this limited period may not be representative of a trend consistent with the results presented or otherwise predictive of future results. We commenced our commercial launch of Vascepa on January 28, 2013. Accordingly, there is a very limited amount of information available at this time to determine the actual number of total prescriptions for Vascepa. We believe investors should consider our results for the first quarter of 2013 and the as-reported Vascepa prescription data from February through June of 2013 together with results over several future quarters, or longer, before making an assessment about potential future performance.

In addition to the factors identified above, seasonal fluctuations in pharmaceutical sales, for example, may affect future prescription trends of Vascepa. The historical prescription data provided in our filings with the SEC are based on data published by a third party as of July 5, 2013. Although we believe these data are prepared on a period-to-period basis in a manner that is generally consistent and that such results are generally indicative of current prescription trends, these data are based on estimates and should not be relied upon as definitive. These data may overstate or understate actual prescriptions. Moreover, in accordance with our revenue recognition policy and U.S. Generally Accepted Account Principles, or GAAP, until we have more experience with the commercialization of Vascepa and can reasonably estimate any product returns, we plan to recognize revenue based on the resale of Vascepa from the distributors to which we sell Vascepa, and not based on sales from us to such distributors. Accordingly, because of our limited selling history, during the quarter ended March 31, 2013, we only recognized revenue on product that we could substantiate being resold by retailers, such as pharmacies, for purposes of fulfilling prescriptions. These prescription data may differ from the data reported by third parties. The value of product shipped to distributors but not resold by the distributors to retailers has been deferred until we have evidence that the product was resold by retailers or until we gain sufficient history with our customers to be able to estimate product returns. This is the case even where invoices for such shipments have been collected in full. From launch through June 30, 2013, we had experienced no material product returns.

We have to compete with other pharmaceutical and life sciences companies to recruit, hire, train and retain sales and marketing personnel, and turnover in our sales force and marketing personnel could negatively affect sales of Vascepa. If we are not successful in our efforts to market and sell Vascepa on our own, market acceptance of Vascepa may be harmed, our anticipated revenues will be materially and negatively impacted, and we may need additional funding or seek a strategic licensing or co-promotion transaction as a means of raising additional funds.

Vascepa may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

We only recently began marketing and selling Vascepa for use in the MARINE indication in January 2013. Vascepa may fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. If Vascepa does not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of Vascepa for the MARINE indication and any future approved indications will depend on a number of factors, including:

the perceived efficacy, safety and potential advantages of Vascepa, as compared to alternative treatments;

our ability to offer Vascepa for sale at competitive prices;

convenience and ease of administration compared to alternative treatments;

the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;

the scope, effectiveness and strength of product education, marketing and distribution support, including our sales and marketing team;

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publicity concerning Vascepa or competing products;

sufficient third-party coverage or reimbursement; and

the actual efficacy of the product and the prevalence and severity of any side effects, including any limitations or warnings contained in Vascepa s approved labeling.

We may not be able to compete effectively against our competitors pharmaceutical products.

The pharmaceutical industry is highly competitive. In attempting to achieve the widespread commercialization of Vascepa, we will face competition to the extent other pharmaceutical companies have on the market, or are able to develop, products for the treatment of similar indications. Potential competitors in this market include companies with greater experience in commercializing pharmaceutical products, and greater resources and name recognition than we have. Furthermore, to the extent we are able to acquire or develop additional marketable products in the future, such products will compete with a variety of other products within the United States or elsewhere, possibly including established drugs and major brand names and also generic versions of these products. Competitive factors, including generic competition, could force us to lower prices or could result in reduced sales. In addition, new products developed by others could emerge as competitors to our future products. Products based on new technologies or new drugs could render our products obsolete or uneconomical.

The success of Vascepa and any of our future products will also depend in large part on the willingness of physicians to prescribe these products to their patients. Vascepa will, and our future products may, compete against products that have achieved broad recognition and acceptance among medical professionals. In order to achieve an acceptable level of prescriptions for Vascepa or any future product, we must be able to meet the needs of both the medical community and end users with respect to cost, efficacy and other factors.

Our potential competitors both in the United States and Europe include large, well-established pharmaceutical companies, specialty pharmaceutical sales and marketing companies, and specialized cardiovascular treatment companies. These companies include GlaxoSmithKline plc, which currently markets Lovaza, a prescription-only omega-3 fatty acid indicated for patients with severe hypertriglyceridemia, and Abbott Laboratories, which currently markets Tricor and Trilipix for the treatment of severe hypertriglyceridemia and mixed dyslipidemia and Niaspan, which is primarily used to raise HDL-C, but is also used to lower triglycerides. In March 2011, Pronova BioPharma Norge AS, now owned by BASF, which owns the patents for Lovaza, entered into an agreement with Apotex Corp. and Apotex Inc. to settle their patent litigation in the United States related to Lovaza. Pursuant to the terms of the settlement agreement, Pronova granted Apotex a license to enter the United States market with a generic version of Lovaza in the first quarter of 2015, or earlier depending on circumstances. We expect Apotex to compete against us as well. Other companies are also seeking to introduce generic versions of Lovaza. These competitors have greater resources than we do, including financial, product development, marketing, personnel and other resources.

In addition, we are aware of other pharmaceutical companies that are developing products that, if approved, would compete with Vascepa. These include a free fatty acid form of omega-3 (comprised of 55% EPA and 20% DHA) that is being developed by Omthera Pharmaceuticals, which in April 2012 announced its top-line Phase 3 clinical trial results and indicated that it plans to submit an NDA during 2013 for the treatment of hypertriglyceridemia. In May 2013, AstraZeneca PLC agreed to acquire Omthera Pharmaceuticals, and AstraZeneca may utilize its substantial commercial resources to market Omthera Pharmaceuticals product, if approved. We also understand that another company, Trygg Pharma AS, has completed a Phase 3 study of an omega-3 based drug candidate for hypertriglyceridemia, but we believe Trygg has not yet announced results from that study. It is possible that Trygg Pharma has filed for FDA approval of its product candidate. In addition, Acasti Pharma, a subsidiary of Neptune Technologies & Bioresources Inc., announced in late 2012 that it intends to conduct a Phase 3 clinical program to assess the safety and efficacy of its omega-3 prescription drug candidate derived from krill oil for the treatment of hypertriglyceridemia. We believe Resolvyx Pharmaceuticals and

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Catabasis Pharmaceuticals are also developing potential treatments for hypertriglyceridemia based on omega-3 fatty acids but, to our knowledge, neither has initiated a Phase 2 clinical trial of its product. In addition, we are aware that Essentialis, Inc is developing a controlled release diazoxide product for the treatment of hypertriglyceridemia and that Matinas BioPharma, Inc. is developing an omega-3-based therapeutic for the treatment of severe hypertriglyceridemia and mixed dyslipidemia. Essentialis, Inc. has reported that they have completed Phase 2 clinical studies with its product. Matinas BioPharma, Inc. has reported that it is preparing to file an Investigational New Drug Application with the FDA and conduct a human study in 2013. Isis Pharmaceuticals recently announced favorable Phase 2 results of ISIS-APOCIII<sub>Rx</sub>, a drug candidate administered through weekly subcutaneous injections, in patients with high triglycerides and type 2 diabetes. Isis is also evaluating ISIS-APOCIII<sub>Rx</sub> in a separate Phase 2 study in patients with moderate to severe high triglycerides and has announced plans to report data from this study in the summer of 2013.

# Competitors may seek approval of generic versions of Vascepa.

In April 2013, the FDA published draft guidance for companies that may seek to develop generic versions of Vascepa. If an application for a generic version of Vascepa were filed and if NCE exclusivity is not granted to Vascepa, the FDA may accept the filing for review and we would likely engage in costly litigation with the applicant to protect our patent rights. If the generic filer is ultimately successful in patent litigation against us, meets the requirements for a generic version of Vascepa to the satisfaction of the FDA (after any applicable regulatory exclusivity period and, typically, the litigation-related 30-month stay period expires), and is able to supply the product in significant commercial quantities, the generic company could, with the market introduction of a generic version of Vascepa, limit our U.S. sales, which would have an adverse impact on our business and results of operations. In addition, even if a competitor s effort to introduce a generic product is ultimately unsuccessful, the perception that such development is in progress and/or news related to such progress could materially affect the perceived value of our company and its stock price.

Vascepa is a prescription-only omega-3 fatty acid. Omega-3 fatty acids are also marketed by other companies as non-prescription dietary supplements. As a result, Vascepa would be subject to non-prescription competition and consumer substitution.

Our only current product, Vascepa, is a prescription-only omega-3 fatty acid. Mixtures of omega-3 fatty acids are naturally occurring substances contained in various foods, including fatty fish. Omega-3 fatty acids are also marketed by others as non-prescription dietary supplements. We cannot be sure physicians will view the pharmaceutical grade purity of Vascepa as having a superior therapeutic profile to naturally occurring omega-3 fatty acids and dietary supplements. To the extent the price of Vascepa is significantly higher than the prices of commercially available omega-3 fatty acids marketed by other companies as dietary supplements (through that lack of coverage by insurers or otherwise), physicians may recommend these commercial alternatives instead of writing prescriptions for Vascepa or patients may elect on their own to take commercially available omega-3 fatty acids. Either of these outcomes may adversely impact our results of operations by limiting how we price our product and limiting the revenue we receive from the sale of Vascepa due to reduced market acceptance.

If we are not successful marketing and selling Vascepa on our own, we may need to find collaborative partners to help market and sell the product.

If we are not successful marketing and selling Vascepa on our own, we may need to find collaborative partners to help market and sell the product or otherwise outsource these functions to third parties. Until such time as we choose to, and actually do, complete a strategic transaction with a third party to market and sell Vascepa, if ever, we will continue to market and sell Vascepa on our own. We are actively exploring collaboration opportunities for the continued marketing and sale of Vascepa as we approach the potential approval of Vascepa in the ANCHOR indication, assuming its regulatory approval.

We may not be successful in finding a collaborative partner to help market and sell Vascepa, or may be delayed in doing so, if we determine such a collaborative partner is necessary, in which case we may not receive

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revenue to the extent that we currently anticipate. We face significant competition in seeking appropriate collaborators, and these collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on acceptable terms, or at all. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If that were to occur, we may have to curtail the continued development of Vascepa for approval for additional indications beyond ANCHOR or increase our planned expenditures and undertake additional development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all, or which may not be possible due to our other financing arrangements, including our Purchase and Sale Agreement with Biopharma Secured Debt Fund II Holdings Cayman, L.P., or Biopharma. If we cannot raise sufficient funds, we may not be able to market and sell Vascepa effectively, and generate as much product revenue, as we could under collaboration.

Our ability to generate increased revenue depends, in part, on FDA approval for the use of Vascepa in the ANCHOR indication in the United States and potentially on other regulatory approvals outside the United States, and we may be delayed in obtaining, or never obtain, such approvals.

The costs involved in obtaining regulatory approvals for pharmaceutical products can be substantial. While we are currently marketing Vascepa for use in the MARINE indication in the United States, our ability to commercialize Vascepa in the ANCHOR indication in the United States or market Vascepa for either indication outside of the United States is dependent upon receiving additional regulatory approvals. In April 2013, the FDA accepted our sNDA which seeks approval for the use of Vascepa in the ANCHOR indication, and the FDA has assigned the sNDA a PDUFA date of December 20, 2013 for the completion of its review. The PDUFA date is the goal date for the FDA to complete its review of the sNDA. However, there can be no assurance that the FDA will complete its review of the sNDA by this date. Additionally, the FDA could deny approval of our sNDA and require additional testing or data. For example, FDA may require that we complete the REDUCE-IT cardiovascular outcome trial before they approve our sNDA. If the FDA takes any of these actions, they could have a material adverse effect on our operations and financial condition, including our ability to reach profitability.

Even if we obtain additional regulatory approvals for Vascepa, the timing or scope of any approvals may prohibit or reduce our ability to commercialize the product successfully. For example, if the approval process for the ANCHOR indication takes too long, we may miss market opportunities and give other companies the ability to develop competing products or establish market dominance. Additionally, the terms of any approvals, including the approval received from the FDA in July 2012 for the MARINE indication, may prove to not have the scope or breadth needed for us to successfully commercialize Vascepa or become profitable.

The FDA advisory committee may render recommendations on the sNDA for the ANCHOR indication that are negative or may delay approval or limit Vascepa s marketability and may raise new concerns.

On June 18, 2013, the FDA informed us that it plans to convene an advisory committee on October 16, 2013 to review the sNDA for the ANCHOR indication. Shortly before the advisory committee meeting, the FDA will publish on its website its executive summary based on its review of the sNDA, which may identify any concerns the agency has with our sNDA. Even if the advisory committee ultimately disagrees with these concerns, the publication of these concerns may negatively affect us. The FDA is not bound by the recommendations of an advisory committee, which is typically composed of clinicians, statisticians and other experts, but it generally follows such recommendations. The advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional preclinical studies or clinical trials, including for example our REDUCE-IT cardiovascular outcomes trial, limitations on approved labeling, or distribution and use restrictions. This may delay and increase the cost of the review process. Although not typically the case, the FDA can, at its option, extend the time for its review of the sNDA for the ANCHOR indication or delay the advisory committee review. Any delay in obtaining, or an inability to obtain, marketing approval could prevent us from commercializing Vascepa in the ANCHOR indication, continuing our REDUCE-IT study, generating revenue, and achieving profitability.

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### Our SPAs with the FDA are not guarantees of FDA approval of Vascepa for the proposed ANCHOR and REDUCE-IT indications.

A Special Protocol Assessment, or SPA, is an evaluation by the FDA of a protocol with the goal of reaching an agreement that the Phase 3 trial protocol design, clinical endpoints, and statistical analyses are acceptable to support regulatory approval of the drug product candidate with respect to effectiveness for the indication studied. The ANCHOR trial was, and the REDUCE-IT trial is, being conducted under an SPA with the FDA. The FDA agreed that, based on the information we submitted to the agency, the design and planned analysis of the ANCHOR trial is adequate to support use of the conducted study as the primary basis for approval with respect to effectiveness. An SPA is generally binding upon the FDA except in limited circumstances, such as if the FDA identifies a substantial scientific issue essential to determining safety or efficacy after the study begins, or if the study sponsor fails to follow the protocol that was agreed upon with the FDA. Even though we have received regulatory approval of Vascepa for the MARINE indication, there is no assurance that the FDA will not identify a scientific issue and deem either or both of the ANCHOR or REDUCE-IT SPAs no longer binding. Moreover, any change to a study protocol after agreement with the FDA is reached can invalidate an SPA. While we amended the protocol for the ANCHOR trial after the initial SPA evaluation was completed, we obtained the FDA sevaluation of, and agreement to, the amendment. If, for example, the FDA does not consider the applicable SPA to be binding during its review of our regulatory approval applications, or if the FDA determines that we did not follow the SPAs appropriately, the agency could assert that additional studies or data are required to support approval of the application. As another example, if the FDA determines that the potential risk of the use of Vascepa outweighs the potential benefit of the drug in the ANCHOR indication, the FDA may choose not to approve Vascepa for use in the ANCHOR population, regardless of our adherenc

## The commercial value to us of the MARINE and ANCHOR indications may be smaller than we anticipate.

There can be no assurance as to the adequacy for commercial success of the scope and breadth of the MARINE indication or, if approved, the ANCHOR indication. Even if we obtain marketing approval for additional indications, the FDA may impose restrictions on the product s conditions for use, distribution or marketing and in some cases may impose ongoing requirements for post-market surveillance, post-approval studies or clinical trials. Also, with regard to the MARINE indication and any other indications for which we may gain approval, the number of actual patients with the condition included in such approved indication may be smaller than we anticipate. If any such approved indication is narrower than we anticipate, the market potential for our product would suffer.

### Our products will be subject to extensive post-approval government regulation.

Once a product candidate receives FDA marketing approval, numerous post-approval requirements apply. Among other things, the holder of an approved NDA is subject to periodic and other monitoring and reporting obligations enforced by the FDA and other regulatory bodies, including obligations to monitor and report adverse events and instances of the failure of a product to meet the specifications in the approved application. Application holders must also submit advertising and other promotional material to regulatory authorities and report on ongoing clinical trials.

With respect to sales and marketing activities including direct-to-consumer advertising and promotional activities involving the Internet, advertising and promotional materials must comply with FDA rules in addition to other applicable federal and local laws in the United States and in other countries. Industry-sponsored scientific and educational activities also must comply with FDA and other requirements. In the United States, the distribution of product samples to physicians must comply with the requirements of the U.S. Prescription Drug Marketing Act. Manufacturing facilities remain subject to FDA inspection and must continue to adhere to the FDA s current good manufacturing practice requirements, or cGMPs. Application holders must obtain FDA approval for product and manufacturing changes, depending on the nature of the change. We also are subject to the new federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, which require manufacturers of certain drugs, devices,

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biologics, and medical supplies to report to the Centers for Medicare & Medicaid Services, or CMS, information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests. We may also be subject, directly or indirectly through our customers and partners, to various fraud and abuse laws, including, without limitation, the U.S. Anti-Kickback Statute, U.S. False Claims Act, and similar state laws, which impact, among other things, our proposed sales, marketing, and scientific/educational grant programs. If we participate in the U.S. Medicaid Drug Rebate Program, the Federal Supply Schedule of the U.S. Department of Veterans Affairs, or other government drug programs, we will be subject to complex laws and regulations regarding reporting and payment obligations. All of these activities are also potentially subject to U.S. federal and state consumer protection and unfair competition laws. Similar requirements exist in many of these areas in other countries.

Depending on the circumstances, failure to meet these post-approval requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, or refusal to allow us to enter into supply contracts, including government contracts. In addition, even if we or our potential partners comply with FDA and other requirements, new information regarding the safety or effectiveness of a product could lead the FDA to modify or withdraw a product approval. Adverse regulatory action, whether pre- or post-approval, can potentially lead to product liability claims and increase our product liability exposure. We or our potential partners must also compete against other products in qualifying for coverage and reimbursement under applicable third party payment and insurance programs.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. If we are found to have improperly promoted off-label uses, we may become subject to significant fines and other liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product s approved labeling. Even though we received marketing approval for Vascepa for the MARINE indication only, physicians may nevertheless prescribe Vascepa to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant government fines and other related liability. For example, the Federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, incentives exist under applicable laws that encourage competitors, employees and physicians to report violations of rules governing promotional activities for pharmaceutical products. These incentives could lead to so-called whistleblower lawsuits as part of which such persons seek to collect a portion of moneys allegedly overbilled to government agencies due to, for example, promotion of pharmaceutical products beyond labeled claims. These incentives could also lead to suits that we have mischaracterized a competitor s product in the marketplace and may, as a result, be sued for alleged damages to our competitors. Such lawsuits, whether with or without merit, are typically time-consuming and costly to defend. Such suits may also result in related shareholder lawsuits, which are also costly to defend.

The REDUCE-IT cardiovascular outcomes trial may fail to show that Vascepa can reduce major cardiovascular events in an at-risk patient population on statin therapy, and the long-term clinical results of Vascepa may not be consistent with the clinical results we observed in our Phase 3 clinical trial, in which case our sales of Vascepa may then suffer.

In accordance with the SPA for our MARINE and ANCHOR trials, efficacy was evaluated in these trials compared to placebo at twelve weeks. No placebo-controlled studies have been conducted regarding the long-

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term effect of Vascepa on lipids, and no outcomes study has been conducted evaluating Vascepa. The REDUCE-IT study is designed to evaluate the efficacy of Vascepa in reducing major cardiovascular events in an at-risk patient population on statin therapy.

Outcomes studies of certain other lipid modifying therapies have failed to achieve the endpoints of such studies. For example, in September 2012, researchers published in the *Journal of the American Medical Association*, or *JAMA*, the results of a retrospective meta-analysis of twenty previously conducted studies regarding the use of omega-3 supplements across various patient populations. This meta-analysis suggested that the use of such supplements was not associated with a lower risk of all-cause death, cardiac death, sudden death, heart attack, or stroke. We believe the results of the JAMA meta-analysis may not be directly applicable to the use of Vascepa over time. For instance, nineteen of the twenty studies included in the JAMA meta-analysis involved the use of omega-3 supplements containing a mixture of EPA and DHA, and most were evaluated at relatively lower doses. In addition, in May 2013, *The New England Journal of Medicine* published the results of an outcome study of 1 gram per day of an omega-3 acid ethyl ester composition. In that study, the composition failed to show a benefit in reducing the rate of death from cardiovascular causes or hospitalization for cardiovascular causes when administered to patients with cardiovascular risk factors under different study conditions than in the REDUCE-IT study. Vascepa is comprised of highly-pure ethyl-EPA, and has been approved by the FDA for use in patients with severe hypertriglyceridemia at a dose of 4 grams per day. The only other outcomes study involving the use of a highly-pure formulation of ethyl-EPA, called the Japan EPA Lipid Intervention Study (JELIS), suggested that use of a highly-pure formulation of ethyl-EPA in Japan, when used in conjunction with statins, reduced cardiovascular events by 19% compared to the use of statins alone.

Although we believe the results of the JAMA meta-analysis and other studies are not directly applicable to the potential long-term clinical experience with Vascepa, there can be no assurance that the endpoints of the REDUCE-IT cardiovascular outcomes study will be achieved or that the lipid modifying effects of Vascepa in REDUCE-IT or any other study of Vascepa will not be subject to variation beyond twelve weeks. If the REDUCE-IT trial fails to achieve its clinical endpoints or if the results of these long-term studies are not consistent with the 12-week clinical results, it could prevent us from expanding the label of any approved product or even call into question the efficacy of any approved product.

We may not be successful in developing or marketing future products if we cannot meet the extensive regulatory requirements of the FDA and other regulatory agencies for quality, safety and efficacy.

The success of our research and development efforts is dependent in part upon our ability, and the ability of our partners or potential partners, to meet regulatory requirements in the jurisdictions where we or our partners or potential partners ultimately intend to sell such products once approved. The development, manufacture and marketing of pharmaceutical products are subject to extensive regulation by governmental authorities in the United States, the European Union, Japan and elsewhere. In the United States, the FDA generally requires pre-clinical testing and clinical trials of each drug to establish its safety and efficacy and extensive pharmaceutical development to ensure its quality before its introduction into the market. Regulatory authorities in other jurisdictions impose similar requirements. The process of obtaining regulatory approvals is lengthy and expensive and the issuance of such approvals is uncertain. The commencement and rate of completion of clinical trials and the timing of obtaining marketing approval from regulatory authorities may be delayed by many factors, including:

the lack of efficacy during clinical trials;

the inability to manufacture sufficient quantities of qualified materials under cGMPs for use in clinical trials;

slower than expected rates of patient recruitment;

the inability to observe patients adequately after treatment;

changes in regulatory requirements for clinical or preclinical studies;

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the emergence of unforeseen safety issues in clinical or preclinical studies;

delay, suspension, or termination of a trial by the institutional review board responsible for overseeing the study at a particular study site:

unanticipated changes to the requirements imposed by regulatory authorities on the extent, nature or timing of studies to be conducted on quality, safety and efficacy; and

government or regulatory delays or clinical holds requiring suspension or termination of a trial.

Even if we obtain positive results from early stage pre-clinical or clinical trials, we may not achieve the same success in future trials. Clinical trials that we or potential partners conduct may not provide sufficient safety and efficacy data to obtain the requisite regulatory approvals for product candidates. The failure of clinical trials to demonstrate safety and efficacy for our desired indications could harm the development of that product candidate as well as other product candidates, and our business and results of operations would suffer. For example, the efficacy results of our Vascepa Phase 3 clinical trials for the treatment of Huntington s disease were negative. As a result, we stopped development of that product candidate, revised our clinical strategy and shifted our focus to develop Vascepa for use in the treatment of cardiovascular disease.

Any approvals that are obtained may be limited in scope, may require additional post-approval studies or may require the addition of labeling statements focusing on product safety that could affect the commercial potential for our product candidates. Any of these or similar circumstances could adversely affect our ability to earn revenues from the sale of such products. Even in circumstances where products are approved by a regulatory body for sale, the regulatory or legal requirements may change over time, or new safety or efficacy information may be identified concerning a product, which may lead to the withdrawal of a product from the market or similar use restrictions. The discovery of previously unknown problems with a product or in connection with the manufacturer of products may result in restrictions on that product or manufacturer, including withdrawal of the product from the market, which would have a negative impact on our potential revenue stream.

Legislative or regulatory reform of the health care system in the United States and foreign jurisdictions may affect our ability to profitably sell Vascepa.

Our ability to commercialize our future products successfully, alone or with collaborators, will depend in part on the extent to which coverage and reimbursement for the products will be available from government and health administration authorities, private health insurers and other third-party payors. The continuing efforts of the U.S. and foreign governments, insurance companies, managed care organizations and other payors of health care services to contain or reduce health care costs may adversely affect our ability to set prices for our products which we believe are fair, and our ability to generate revenues and achieve and maintain profitability.

Specifically, in both the United States and some foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the health care system in ways that could affect our ability to sell our products profitably. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the PPACA, enacted in March 2010, substantially changes the way healthcare is financed by both governmental and private insurers. Among other cost-containment measures, PPACA establishes:

An annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents;

A new Medicare Part D coverage gap discount program, in which pharmaceutical manufacturers who wish to have their drugs covered under Part D must offer discounts to eligible beneficiaries during their coverage gap period; and

A new formula that increases the rebates a manufacturer must pay under the Medicaid Drug Rebate Program.

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We expect further federal and state proposals and health care reforms to continue to be proposed by legislators, which could limit the prices that can be charged for the products we develop and may limit our commercial opportunity.

The continuing efforts of government and other third-party payors to contain or reduce the costs of health care through various means may limit our commercial opportunity. It will be time consuming and expensive for us to go through the process of seeking coverage and reimbursement from Medicare and private payors. Our products may not be considered cost effective, and government and third-party private health insurance coverage and reimbursement may not be available to patients for any of our future products or sufficient to allow us to sell our products on a competitive and profitable basis. Our results of operations could be adversely affected by PPACA and by other health care reforms that may be enacted or adopted in the future. In addition, increasing emphasis on managed care in the United States will continue to put pressure on the pricing of pharmaceutical products. Cost control initiatives could decrease the price that we or any potential collaborators could receive for any of our future products and could adversely affect our profitability.

In some foreign countries, including major markets in the European Union and Japan, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take 6 to 12 months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a pharmacoeconomic study that compares the cost-effectiveness of Vascepa to other available therapies. Such pharmacoeconomic studies can be costly and the results uncertain. Our business could be harmed if reimbursement of our products is unavailable or limited in scope or amount or if pricing is set at unsatisfactory levels.

As we evolve from a company primarily involved in research and development to a company also focused on establishing an infrastructure for commercializing Vascepa, we may encounter difficulties in managing our growth and expanding our operations successfully.

We only recently hired and trained a professional sales force of approximately 275 sales representatives and commenced our commercial launch of Vascepa in the MARINE indication in the United States in early January 2013. The process of establishing a commercial infrastructure is difficult, expensive and time-consuming. As our operations expand, we expect that we will need to manage additional relationships with various collaborative partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. Our future financial performance and our ability to commercialize Vascepa and to compete effectively will depend, in part, on our ability to manage our future growth effectively. To that end, we must be able to manage our development efforts effectively, and hire, train, integrate and retain additional management, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

### Risks Related to our Reliance on Third Parties

Our supply of product for commercial supply and clinical trials is dependent upon relationships with third party manufacturers and key suppliers.

We have no in-house manufacturing capacity and rely on contract manufacturers for our clinical and commercial product supply. We cannot assure you that we will successfully manufacture any product we may develop, either independently or under manufacturing arrangements, if any, with our third party manufacturers. Moreover, if any manufacturer should cease doing business with us or experience delays, shortages of supply or excessive demands on their capacity, we may not be able to obtain adequate quantities of product in a timely manner, or at all.

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Any manufacturing problem, natural disaster affecting manufacturing facilities, or the loss of a contract manufacturer could be disruptive to our operations and result in lost sales. Additionally, we will be reliant on third parties to supply the raw materials needed to manufacture our potential products. Any reliance on suppliers may involve several risks, including a potential inability to obtain critical materials and reduced control over production costs, delivery schedules, reliability and quality. Any unanticipated disruption to future contract manufacture caused by problems at suppliers could delay shipment of products, increase our cost of goods sold and result in lost sales. If our suppliers were unable to supply us with adequate supply of ethyl-EPA it would have a material adverse effect on our ability to continue to commercialize Vascepa.

We initially purchased all of our supply of the bulk compound (ethyl-EPA), which constitutes the only active pharmaceutical ingredient, or API, of Vascepa, from a single supplier, Nisshin Pharma, or Nisshin, located in Japan. Nisshin was approved by the FDA as a Vascepa API supplier as part of our FDA marketing approval for the MARINE indication in July 2012. In April 2013, we announced the approval by the FDA of Chemport, Inc. and BASF as additional Vascepa API suppliers. We now plan to use and purchase additional commercial supply from Chemport and BASF (formerly Equateq Limited) in addition to Nisshin. Each of the API manufacturers obtains supply of the key raw material to manufacture API from other third party sources of supply.

While we have contractual freedom to source the API for Vascepa and have entered into supply agreements with multiple suppliers who also rely on other third party suppliers of the key raw material to manufacture the API for Vascepa, Nisshin currently supplies a large majority of our API for Vascepa. Our strategy in adding API suppliers beyond Nisshin has been to expand manufacturing capacity and to partially mitigate the risk of reliance on one supplier Both Chemport and BASF continue to expand their API manufacturing capacity and bring to three the number of qualified worldwide suppliers of API for Vascepa.

Also, in December 2012 we announced the addition of an exclusive consortium of companies led by Slanmhor Pharmaceutical, Inc., or Slanmhor, to our planned API global supply chain for Vascepa. Slanmhor was spun-out from Ocean Nutrition Canada, or ONC, prior to the May 2012 acquisition of ONC by Royal DSM N.V., a global leader in life sciences and materials sciences. Amarin now has a total of four suppliers for Vascepa API to utilize in supporting the global commercialization of Vascepa, subject to appropriate regulatory approval of Slanmhor. We intend to submit an additional sNDA for Slanmhor after it successfully completes the qualification process.

Expanding manufacturing capacity and qualifying such capacity is difficult and subject to numerous regulations and other operational challenges. The resources of our suppliers are limited and costs associated with projected expansion and qualification can be significant. The resources of our suppliers vary. For example, Chemport, which was approved as one of our API supplier in April 2013, is a privately-held company and their commitment to Vascepa supply has required them to seek additional resources. There can be no assurance that the expansion plans of any of our suppliers will be successful. Our aggregate capacity to produce API is dependent upon the qualification of our API suppliers. Each of our API suppliers has outlined plans for potential further capacity expansion. If no additional API supplier is approved by the FDA, our API supply will be limited to the API we purchase from Nisshin, Chemport and BASF. If our third party manufacturing capacity is not expanded and compliant with application regulatory requirements, we may not be able to supply sufficient quantities of Vascepa to meet anticipated demand. We cannot assure you that we can contract with any future manufacturer on acceptable terms or that any such alternative supplier will not require capital investment from us in order for them to meet our requirements. Alternatively, our purchase of supply may exceed actual demand for Vascepa.

We currently rely on two suppliers, Banner and Catalent, for the encapsulation of API for all capsules of Vascepa. While we have contractual freedom to source the API encapsulation for Vascepa elsewhere, Banner and Catalent are the only encapsulators approved by the FDA for encapsulation of API for Vascepa. There can be no guarantee that additional other suppliers with which we have contracted to encapsulate API will be qualified to

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manufacture the product to our specifications or that these and any future suppliers will have the manufacturing capacity to meeting anticipated demand for Vascepa. We cannot assure you that we can contract with any future manufacturer on acceptable terms or that any such alternative supplier will not require capital investment from us in order for them to meet our requirements.

We do not have sufficient experience with the commercial sale of Vascepa, and such inexperience may cause us to purchase too much or not enough supply to satisfy actual demand, which could have a material adverse effect on our financial results and financial condition.

Our agreements with our suppliers typically include minimum purchase obligations and limited exclusivity provisions. These purchases are generally made on the basis of rolling twelve-month forecasts which in part are binding on us and the balance of which are subject to adjustment by us subject to certain limitations. We have no experience with the commercial sale of Vascepa, and as such expectations regarding expected demand may be wrong. We may not purchase sufficient quantities of Vascepa to meet actual demand or our purchase of supply may exceed actual demand. In either case, such event could have a material adverse effect on our financial results and financial condition.

The manufacture and packaging of pharmaceutical products such as Vascepa are subject to FDA requirements and those of similar foreign regulatory bodies. If we or our third party manufacturers fail to satisfy these requirements, our product development and commercialization efforts may be materially harmed.

The manufacture and packaging of pharmaceutical products, such as Vascepa, are regulated by the FDA and similar foreign regulatory bodies and must be conducted in accordance with the FDA s cGMPs and comparable requirements of foreign regulatory bodies. There are a limited number of manufacturers that operate under these cGMPs regulations who are both capable of manufacturing Vascepa and willing to do so. Failure by us or our third party manufacturers to comply with applicable regulations, requirements, or guidelines could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our products, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business. For example, Nisshin plans to expand it capacity to supply API to us by further expanding their current facility. If we are not able to manufacture Vascepa to required specifications through Nisshin, Chemport and BASF, or other potential API suppliers, we may be delayed in successfully supplying the product to meet anticipated demand and our anticipated future revenues and financial results may be materially adversely affected.

Changes in the manufacturing process or procedure, including a change in the location where the product is manufactured or a change of a third party manufacturer, may require prior FDA review and approval of the manufacturing process and procedures in accordance with the FDA s cGMPs, or cGMPs. Any new facility may be subject to a pre-approval inspection by the FDA and would again require us to demonstrate product comparability to the FDA. There are comparable foreign requirements. This review may be costly and time consuming and could delay or prevent the launch of a product. For example, we have plans to file a supplemental NDA to add Slanmhor as an additional API supplier for Vascepa. If Slanmhor cannot establish, to the satisfaction of the FDA, that it is in substantial compliance with cGMPs, and that the products manufactured at its site meets FDA requirements, we may not be able to manufacture API from that site, our supply of API for Vascepa may be delayed, and our anticipated future revenues and financial results may be materially adversely affected if such supply cannot be satisfied by our other three API suppliers.

Furthermore, the FDA and foreign regulatory agencies require that we be able to consistently produce the API and the finished product in commercial quantities and of specified quality on a repeated basis, including proven product stability, and document our ability to do so. This requirement is referred to as process validation. This includes stability testing, measurement of impurities and testing of other product specifications by validated

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test methods. If the FDA does not consider the result of the process validation or required testing to be satisfactory, the commercial supply of Vascepa may be delayed, or we may not be able to supply sufficient quantities of Vascepa to meet anticipated demand.

The FDA and similar foreign regulatory bodies may also implement new standards, or change their interpretation and enforcement of existing standards and requirements, for manufacture, packaging or testing of products at any time. If we are unable to comply, we may be subject to regulatory, civil actions or penalties which could significantly and adversely affect our business.

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of such clinical trials.

Our reliance on third parties for clinical development activities reduces our control over these activities. However, if we sponsor clinical trials, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties does not relieve us of these responsibilities and requirements. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be delayed in obtaining regulatory approvals for our product candidates and may be delayed in our efforts to successfully commercialize our product candidates for targeted diseases.

### Risks Related to our Intellectual Property and Regulatory Exclusivity

We are dependent on patents, proprietary rights and confidentiality to protect the commercial potential of Vascepa.

Because of the significant time and expense involved in developing new products and obtaining regulatory approvals, it is very important to obtain patent and preserve trade secret protection for new technologies, products and processes. Our ability to successfully implement our business plan will depend in large part on our ability to:

obtain, defend and maintain patent protection and market exclusivity for our current and future products;

preserve any trade secrets relating to our current and future products;

acquire patented or patentable products and technologies; and

operate without infringing the proprietary rights of third parties.

As of May 31, 2013, we have announced that 23 patent applications in the United States have been either issued or allowed and more than 30 additional patent applications are pending in the United States. Of such 23 allowed and issued applications, we currently have

2 issued U.S. patents directed to a pharmaceutical composition of Vascepa in a capsule that have terms that expire in 2020 and 2030, respectively,

1 issued U.S. patent covering a composition containing highly pure EPA that expires in 2021,

14 U.S. patents covering the use of Vascepa in either the MARINE or anticipated ANCHOR indication that have terms that expire in 2030, and

6 additional patent applications for which the United States Patent and Trademark Office, or USPTO, has issued a Notice of Allowance each of which with terms that expire in 2030 and are related to the use of Vascepa in either the MARINE or anticipated ANCHOR indication.

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A Notice of Allowance is issued after the USPTO makes a determination that a patent can be granted from an application. A Notice of Allowance does not afford patent protection until the underlying patent is issued by the USPTO. No assurance can be given that our issued patents and our pending patents, if and when issued, will prevent competitors from competing with Vascepa.

We are also pursuing patent applications related to Vascepa in multiple jurisdictions outside the United States. We may be dependent in some cases upon third party licensors to pursue filing, prosecution and maintenance of patent rights or applications owned or controlled by those parties. It is possible that third parties will obtain patents or other proprietary rights that might be necessary or useful to us. In cases where third parties are first to invent a particular product or technology, or first to file after various provisions of the America Invents Act of 2011 went into effect on March 16, 2013, it is possible that those parties will obtain patents that will be sufficiently broad so as to prevent us from utilizing such technology or commercializing our current and future products.

Although we intend to make reasonable efforts to protect our current and future intellectual property rights and to ensure that any proprietary technology we acquire or develop does not infringe the rights of other parties, we may not be able to ascertain the existence of all potentially conflicting claims. Therefore, there is a risk that third parties may make claims of infringement against our current or future products or technologies. In addition, third parties may be able to obtain patents that prevent the sale of our current or future products or require us to obtain a license and pay significant fees or royalties in order to continue selling such products.

We may in the future discover the existence of products that infringe patents that we own or that have been licensed to us. If we were to initiate legal proceedings against a third party to stop such an infringement, such proceedings could be costly and time consuming, regardless of the outcome. No assurances can be given that we would prevail, and it is possible that, during such a proceeding, our patent rights could be held to be invalid, unenforceable or both. Although we intend to protect our trade secrets and proprietary know-how through confidentiality agreements with our manufacturers, employees and consultants, we may not be able to prevent parties subject to such confidentiality agreements from breaching these agreements or third parties from independently developing or learning of our trade secrets.

We anticipate that competitors may from time to time oppose our efforts to obtain patent protection for new technologies or to submit patented technologies for regulatory approvals. Competitors may seek to oppose our patent applications to delay the approval process or to challenge our granted patents, for example, by requesting a reexamination of our patent at the USPTO, or by filing an opposition in a foreign patent office, even if the opposition or challenge has little or no merit. Such proceedings are generally highly technical, expensive, and time consuming, and there can be no assurance that such a challenge would not result in the narrowing or complete revocation of any patent of ours that was so challenged.

Our issued patents and our pending patents, if and when issued, may not prevent competitors from competing with Vascepa.

We plan to vigorously defend our rights under issued patents. Other drug companies may challenge the validity, enforceability, or both of our patents and seek to design its products around our issued patent claims and gain marketing approval for generic versions of Vascepa or branded competitive products based on new clinical studies. The pharmaceutical industry is highly competitive and many of our competitors have greater experience and resources than we have. Any such competition could undermine sales, marketing and collaboration efforts for Vascepa, and thus reduce, perhaps materially, the revenue potential for Vascepa.

Even if we are successful in enforcing our issued patents, we may incur substantial costs and divert management s time and attention in pursuing these proceedings, which could have a material adverse effect on us. Patent litigation is costly and time consuming, and we may not have sufficient resources to bring these actions to a successful conclusion.

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There can be no assurance that any of our pending patent applications relating to Vascepa or its use will issue as patents.

We have filed and are prosecuting numerous families of patent applications in the United States and internationally with claims designed to protect the proprietary position of Vascepa. For certain of these patent families, we have filed multiple patent applications. Collectively the patent applications include numerous independent claims and dependent claims. Several of our patent applications contain claims that are based upon what we believe are unexpected and favorable findings from the MARINE and ANCHOR trials. If granted, many of the resulting granted patents would expire in 2030 or beyond. However, no assurance can be given that any of our pending patent applications will be granted or, if they grant, that they will prevent competitors from competing with Vascepa.

Securing patent protection for a product is a complex process involving many legal and factual questions. The patent applications we have filed in the United States and internationally are at varying stages of examination, the timing of which is outside our control. The process to getting a patent granted can be lengthy and claims initially submitted are often modified in order to satisfy the requirements of the patent office. This process includes written and public communication with the patent office. The process can also include direct discussions with the patent examiner. There can be no assurance that the patent office will accept our arguments with respect to any patent application or with respect to any claim therein. The timing of the patent review process is independent of and has no effect on the timing of the FDA s review of our NDA or SNDA submissions. We cannot predict the timing or results of any patent application. In addition, we may elect to submit, or the patent office may require, additional evidence to support certain of the claims we are pursuing. Furthermore, third parties may attempt to submit publications for consideration by the patent office during examination of our patent applications. Providing such additional evidence and publications could prolong the patent office s review of our applications and result in us incurring additional costs. We cannot be certain what commercial value any granted patent in our patent estate will provide to us.

#### If Vascepa is not granted new chemical entity exclusivity protection from the FDA our business may be materially harmed.

Under Sections 505(c)(3)(E)(ii) and 505(j)(5)(F)(ii) of the Food Drug and Cosmetic Act, or FDCA, as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, as amended, or the Hatch-Waxman Amendments, a drug that is granted regulatory approval may be eligible for five years of marketing exclusivity in the United States following regulatory approval if that drug is classified as a new chemical entity, or NCE. A drug can be classified as a NCE if the FDA has not previously approved any other drug containing the same active moiety.

The FDA typically publishes a determination on the marketing exclusivity of recently approved products in a cumulative supplement to its *Approved Drug Products with Therapeutic Equivalence Evaluations*, also known as the Orange Book, mid-month in the month following the drug s approval. Vascepa was approved by the FDA in July 2012, but we have not yet been informed of a determination by the FDA on our pending exclusivity request for Vascepa. Since prior to FDA approval of the Vascepa new drug application, we have had an active dialogue with the FDA related to our marketing exclusivity request for Vascepa, which requested NCE status for Vascepa. We have repeatedly followed up with the FDA seeking a determination. While we continue to believe our arguments in support of an NCE determination for Vascepa are strong, the FDA may not agree with our arguments. Based on our discussions with the FDA, we have not been told and do not know what determination the FDA will reach regarding the pending exclusivity request for Vascepa or when the FDA will make such determination. Based on our communications with the FDA, we cannot make a reliable prediction as to when the FDA will communicate a determination on the matter. There can be no assurance that Vascepa will be granted NCE exclusivity, or that the FDA will make a determination on the pending exclusivity request in a timely manner.

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NCE marketing exclusivity, if granted, would preclude approval during the five-year exclusivity period of certain 505(b)(2) applications or abbreviated new drug applications submitted by another company for another version of the drug. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. In this case, Amarin may be afforded the benefit of a 30-month stay against the launch of such a competitive product that would extend from the end of the five-year exclusivity period, and may also be afforded other extensions under applicable regulations, including a six-month pediatric exclusivity extension or a judicial extension if applicable requirements are met. If we are not able to gain or exploit the period of marketing exclusivity, we may face significant competitive threats to our commercialization of these compounds from other manufacturers, including the manufacturers of generic alternatives. Further, even if Vascepa is considered to be a NCE and we are able to gain five-year marketing exclusivity, another company could challenge that decision to seek to overturn FDA s determination. Another company could also gain such marketing exclusivity under the provisions of the FDCA, as amended by the Hatch-Waxman Amendments, if such company can, under certain circumstances, complete a human clinical trial process and obtain regulatory approval of its product.

If Vascepa is not granted NCE marketing exclusivity, we expect it will be granted three years of new product exclusivity under the Hatch-Waxman Amendments. A three-year period of exclusivity is granted under the Hatch-Waxman Amendments for a drug product that contains an active moiety that has been previously approved when the application contains reports of new clinical investigations (other than bioavailability studies) conducted by the sponsor that were essential to approval of the application. Our MARINE trial was a new clinical investigation that was essential to the approval of our new drug application. We are entitled to at least three-year exclusivity even if the FDA determines that the EPA moiety was previously approved in Lovaza because our MARINE clinical investigation was essential for the approval of our new drug product, Vascepa.

Such three-year exclusivity protection would preclude the FDA from approving a marketing application for a duplicate of Vascepa, a product candidate that the FDA views as having the same conditions of approval as Vascepa (for example, the same indication and/or other conditions of use), or a 505(b)(2) NDA submitted to the FDA with Vascepa as the reference product, for a period of three years from the date of FDA approval, although the FDA may accept and commence review of such applications during the exclusivity period. Such three-year exclusivity grant would not prevent a company from challenging the validity of our patents at any time. In this case, Amarin may be afforded the benefit of a 30-month stay against the launch of such a competitive product that would extend from the period that Amarin responds to a pending patent challenge, and may also be afforded other extensions under applicable regulations, including a six-month pediatric exclusivity extension or a judicial extension if applicable requirements are met. This three-year form of exclusivity may also not prevent the FDA from approving an NDA that relies only on its own data to support the change or innovation.

Despite the use of confidentiality agreements and/or proprietary rights agreements, which themselves may be of limited effectiveness, it may be difficult for us to protect our trade secrets.

We will also rely upon trade secrets and know-how to help protect our competitive position. We rely on trade secrets to protect technology in cases when we believe patent protection is not appropriate or obtainable. However, trade secrets are difficult to protect. While we require certain of our academic collaborators, contractors and consultants to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary information.

### Risks Related to our Business

Potential technological changes in our field of business create considerable uncertainty.

We are engaged in the biopharmaceutical field, which is characterized by extensive research efforts and rapid technological progress. New developments in research are expected to continue at a rapid pace in both industry and academia. We cannot assure you that research and discoveries by others will not render some or all of our programs or product candidates uncompetitive or obsolete. Our business strategy is based in part upon new

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and unproven technologies to the development of therapeutics to improve cardiovascular health. We cannot assure you that unforeseen problems will not develop with these technologies or applications or that any commercially feasible products will ultimately be developed by us.

### We are subject to potential product liability.

Following the commercial launch of Vascepa, we will be subject to the potential risk of product liability claims relating to the manufacturing and marketing of Vascepa. Any person who is injured as a result of using Vascepa may have a product liability claim against us without having to prove that we were at fault.

In addition, we could be subject to product liability claims by persons who took part in clinical trials involving our current or former development stage products. A successful claim brought against us could have a material adverse effect on our business. We cannot guarantee that a product liability claim will not be asserted against us in the future.

### We may become subject to liability in connection with the wind-down of our EN101 program.

In 2007, we purchased Ester Neurosciences Limited, an Israeli pharmaceutical company, and its lead product candidate, EN101, an AChE-R mRNA inhibitor for the treatment of myasthenia gravis, or MG, a debilitating neuromuscular disease. In connection with the acquisition, we assumed a license to certain intellectual property assets related to EN101 from the Yissum Research Development Company of The Hebrew University of Jerusalem.

In June 2009, in keeping with our decision to re-focus our efforts on developing improved treatments for cardiovascular disease and cease development of all product candidates outside of our cardiovascular disease focus, we amended the terms of our acquisition agreement with the original shareholders of Ester. Under the terms of this amendment, Amarin was released from all research and development diligence obligations contained in the original agreement and was authorized to seek a partner for EN101. The amendment agreement also provided that any future payment obligations payable by us to the former shareholders of Ester would be made only out of income received from potential partners. In connection with this amendment agreement, in August 2009 we issued 1,315,789 ordinary shares to the former Ester shareholders. Under the terms of this amendment agreement, the former Ester shareholders have the option of reacquiring the original share capital of Ester if we are unable to successfully partner EN101.

Following our decision to cease development of EN101, Yissum terminated its license agreement with us. In June 2011, Yissum announced that it had entered into a license agreement with BiolineRX Ltd for the development of EN101 in a different indication, inflammatory bowel disease.

We have received several communications on behalf of the former shareholders of Ester asserting that we are in breach of its amended agreement due to the fact that Yissum terminated its license and we failed to return shares of Ester, and assets relating to EN101, to the shareholders, as was required under certain circumstances under the amended agreement. We do not believe these circumstances constitute a breach of the amended agreement, but there can be no assurance as to the outcome of this dispute.

## A change in our tax residence could have a negative effect on our future profitability.

Under current UK legislation, a company incorporated in England and Wales, or which is centrally managed and controlled in the UK, is regarded as resident in the UK for taxation purposes. Under current Irish legislation, a company is regarded as resident for tax purposes in Ireland if it is centrally managed and controlled in Ireland, or, in certain circumstances, if it is incorporated in Ireland. Where a company is treated as tax resident under the domestic laws of both the UK and Ireland then the provisions of article 4(3) of the Double Tax Convention between the UK and Ireland provides that such enterprise shall be treated as resident only in the jurisdiction in which its place of effective management is situated. We have sought to conduct our affairs in such a way so as to

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be resident only in Ireland for tax purposes by virtue of having our place of effective management situated in Ireland. Trading income of an Irish company is generally taxable at the Irish corporation tax rate of 12.5%. Non-trading income of an Irish company (e.g., interest income, rental income or other passive income), is taxable at a rate of 25%.

However, we cannot assure you that we are or will continue to be resident only in Ireland for tax purposes. It is possible that in the future, whether as a result of a change in law or the practice of any relevant tax authority or as a result of any change in the conduct of our affairs, we could become, or be regarded as having become resident in a jurisdiction other than Ireland. Should we cease to be an Irish tax resident, we may be subject to a charge to Irish capital gains tax on our assets. Similarly, if the tax residency of any of our subsidiaries were to change from their current jurisdiction for any of the reasons listed above, we may be subject to a charge to local capital gains tax charge on the assets.

### The loss of key personnel could have an adverse effect on our business.

We are highly dependent upon the efforts of our senior management. The loss of the services of one or more members of senior management could have a material adverse effect on us. As a small company with a streamlined management structure, the departure of any key person could have a significant impact and would be potentially disruptive to our business until such time as a suitable replacement is hired. Furthermore, because of the specialized nature of our business, as our business plan progresses we will be highly dependent upon our ability to attract and retain qualified scientific, technical and key management personnel. As we evolve from a development stage company to a commercial stage company we may experience turnover among members of our senior management team. We may have difficulty identifying and integrating new executives to replace any such losses. There is intense competition for qualified personnel in the areas of our activities. In this environment, we may not be able to attract and retain the personnel necessary for the development of our business, particularly if we do not achieve profitability. The failure to recruit key scientific, technical and management personnel would be detrimental to our ability to implement our business plan.

### Risks Related to our Financial Position and Capital Requirements

### We have a history of losses and anticipate that we will incur continued losses for an indefinite period of time.

We have not been profitable in any of the last five fiscal years. For the fiscal years ended December 31, 2012, 2011, and 2010, we reported losses of approximately \$179.2 million, \$69.1 million and \$249.6 million, respectively, and we had an accumulated deficit at December 31, 2012 of \$747.6 million. For the three months ended March 31, 2013 and 2012, we reported losses of approximately \$62.2 million and \$88.3 million, respectively, and we had an accumulated deficit at March 31, 2013 of \$809.8 million. Substantially all of our operating losses resulted from costs incurred in connection with our research and development programs, from general and administrative costs associated with our operations, and from non-cash losses on changes in the fair value of warrant derivative liabilities. Additionally, as a result of our significant expenses relating to research and development and to commercialization, we expect to continue to incur significant operating losses for an indefinite period, even after we begin to generate revenues from our commercialization of Vascepa. Because of the numerous risks and uncertainties associated with developing and commercializing pharmaceutical products, we are unable to predict the magnitude of these future losses. Our historic losses, combined with expected future losses, have had and will continue to have an adverse effect on our cash resources, shareholders deficit and working capital. We expect our research and development expenses to be substantial for both 2013 and 2014 in connection with our REDUCE-IT cardiovascular outcomes study for Vascepa and other activities. In addition, we may incur significant sales, marketing, in-licensing and outsourced manufacturing expenses as we attempt to commercialize Vascepa. Our shift in focus from research and development to commercialization, and the changes in operating costs relating to that shift, will also require us to make changes to our accounting results and procedures, which may have an adverse effect on our reported revenue or profi

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Although we began generating revenue from Vascepa in January 2013, we may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. In January 2013, we began to generate revenue from the marketing of Vascepa for use in the MARINE indication, but we may not be able to generate sufficient revenue to attain profitability. Our ability to generate profits on sales of Vascepa is subject to the market acceptance and commercial success of Vascepa and our ability to manufacture commercial quantities of Vascepa through third parties at acceptable cost levels, and may also depend upon our ability to enter into one or more strategic collaborations to effectively market and sell Vascepa.

Even though Vascepa has been approved by the FDA for marketing in the United States in the MARINE indication, it may not gain market acceptance or achieve commercial success and it may never be approved for the ANCHOR indication or any other indication. In addition, we anticipate continuing to incur significant costs associated with commercializing Vascepa. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate sufficient product revenues, we will not become profitable and may be unable to continue operations without continued funding.

Our historical financial results do not form an accurate basis for assessing our current business.

As a consequence of the many years developing Vascepa for commercialization and the recent commercial launch of Vascepa in the MARINE indication in the United States, our historical financial results do not form an accurate basis upon which investors should base their assessment of our business and prospects. In addition, we expect that our costs will increase substantially as we continue to commercialize Vascepa in the MARINE indication and seek to obtain additional regulatory approval of Vascepa in the ANCHOR indication, including the continuation of the REDUCE-IT cardiovascular outcomes study. Accordingly, our historical financial results reflect a substantially different business from that currently being conducted and from that expected in the future. In addition, we have a limited history of obtaining regulatory approval for, and no demonstrated ability to successfully commercialize, a product candidate. Consequently, any predictions about our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

Our operating results are unpredictable and may fluctuate. If our operating results are below the expectations of securities analysts or investors, the trading price of our stock could decline.

Our operating results are difficult to predict and will likely fluctuate from quarter to quarter and year to year, and Vascepa prescription figures will likely fluctuate from month to month. Due to the recent approval by the FDA of Vascepa and the lack of historical sales data, Vascepa sales will be difficult to predict from period to period and as a result, you should not rely on Vascepa sales results in any period as being indicative of future performance, and sales of Vascepa may be below the expectation of securities analysts or investors in the future. We believe that our quarterly and annual results of operations may be affected by a variety of factors, including:

the level of demand for Vascepa;

the extent to which coverage and reimbursement for Vascepa is available from government and health administration authorities, private health insurers, managed care programs and other third-party payers;

the timing, cost and level of investment in our sales and marketing efforts to support Vascepa sales and the resulting effectiveness of those efforts:

additional developments regarding our intellectual property portfolio and regulatory exclusivity protections, if any; and

the results of our sNDA application for the ANCHOR indication and the results of the REDUCE-IT study or post-approval studies for Vascepa.

We may require substantial additional resources to fund our operations. If we cannot find additional capital resources, we will have difficulty in operating as a going concern and growing our business.

We currently operate with limited resources. At May 31, 2013, we had cash and cash equivalents of approximately \$159.7 million. We believe that our current resources will be sufficient to fund our projected operations for at least the next twelve months, which projected operations contemplate not only working capital and general corporate needs but also the continued commercial launch of Vascepa for the MARINE indication, commercial launch of Vascepa for the ANCHOR indication, if approved, and the advancement of the REDUCE-IT cardiovascular outcomes study.

In order to fund our commercialization plans, in particular to fully support the launch, marketing and sale of Vascepa in the ANCHOR indication, we will likely need to enter into a strategic collaboration or raise additional capital. We will also need additional capital to fully complete our REDUCE-IT cardiovascular outcomes trial.

Our future capital requirements will depend on many factors, including:

revenue generated from the commercial sale of Vascepa in the MARINE indication and, subject to FDA approval, the ANCHOR indication:

the costs associated with commercializing Vascepa for the MARINE indication in the United States and for additional indications in the United States and in jurisdictions in which we receive regulatory approval, if any, including the cost of sales and marketing capabilities, and the cost and timing of securing commercial supply of Vascepa and the timing of entering into strategic collaboration with others relating to the commercialization of Vascepa, if at all, and the terms of any such collaboration;

the continued cost associated with our REDUCE-IT cardiovascular outcomes study;

the time and costs involved in obtaining additional regulatory approvals for Vascepa;

the extent to which we continue to develop internally, acquire or in-license new products, technologies or businesses; and

the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights. If adequate funds are not available to us in amounts or on terms acceptable to us or on a timely basis, or at all, and we do not enter into a collaboration agreement to help support the commercialization of Vascepa, our commercialization efforts for Vascepa may suffer materially, and we may need to delay the advancement of the REDUCE-IT cardiovascular outcomes trial.

Continued negative economic conditions would likely have a negative impact on our ability to obtain financing on acceptable terms.

While we may seek additional funding through public or private financings, we may not be able to obtain financing on acceptable terms, or at all. There can be no assurance that we will be able to access equity or credit markets in order to finance our current operations or expand development programs for Vascepa, or that there will not be a further deterioration in financial markets and confidence in economies. We may also have to scale back or further restructure our operations. If we are unable to obtain additional funding on a timely basis, we may be required to curtail or terminate some or all of our research or development programs or our commercialization strategies.

Raising additional capital may cause dilution to our existing shareholders, restrict our operations or require us to relinquish rights.

To the extent we are permitted under our Purchase and Sale Agreement with Biopharma, we may seek additional capital through a combination of private and public equity offerings, debt financings and collaboration, strategic and licensing arrangements. To the extent that we raise additional capital through the sale of equity or

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convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a shareholder.

As of June 30, 2013, there were warrants outstanding for the purchase of up to 9,866,826 ADSs each representing one of our ordinary shares, with a weighted average exercise price of \$1.44 per share. We may issue additional warrants to purchase ADSs or ordinary shares in connection with any future financing we may conduct. In addition, on January 9, 2012, we issued \$150 million in aggregate principal amount of 3.50% exchangeable senior notes due 2032, or the notes. The notes are exchangeable under certain circumstances into cash, our ADS, or a combination of cash and ADS, at our election, with a current exchange rate of 113.4752 ADS per \$1,000 principal amount of notes. Although we intend to settle these notes in cash, if we elected physical settlement, the notes would initially be exchangeable into 17,021,280 ADS.

Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic alliance and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, Vascepa or product candidates beyond the rights we have already relinquished, or grant licenses on terms that are not favorable to us.

Potential business combinations or other strategic transactions may disrupt our business or divert management s attention.

On a regular basis, we explore potential business combination transactions, including an acquisition of us by a third party, exclusive licenses of Vascepa or other strategic transactions or collaborations with third parties. The consummation and performance of any such future transactions or collaborations will involve risks, such as:

diversion of managerial resources from day-to-day operations;

exposure to litigation from the counterparties to any such transaction, other third parties or our shareholders;

misjudgment with respect to the value;

higher than expected transaction costs; or

an inability to successfully consummate any such transaction or collaboration.

As a result of these risks, we may not be able to achieve the expected benefits of any such transaction or collaboration or deliver the value thereof to our shareholders. If we are unsuccessful in consummating any such transaction or collaboration, we may be required to reevaluate our business only after we have incurred substantial expenses and devoted significant management time and resources.

### Risks Related to Ownership of our ADSs and Common Shares

### The price of our ADSs and common shares may be volatile.

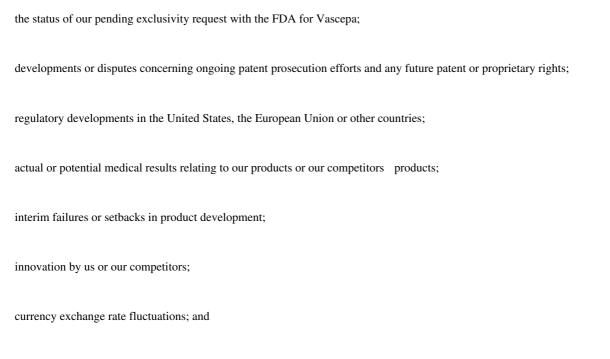
The stock market has from time to time experienced significant price and volume fluctuations that may be unrelated to the operating performance of particular companies. In addition, the market prices of the securities of many pharmaceutical and medical technology companies have been especially volatile in the past, and this trend is expected to continue in the future.

As of June 30, 2013 we had 150,732,881 common shares outstanding. As of June 30, 2013 there were 150,334,422 shares held as ADSs and 398,459 held as common shares (which are not held in the form of ADSs). In our October 2009 private placement we issued 66.4 million ADSs and warrants to purchase an additional 33.2 million ADSs. There is a risk that there may not be sufficient liquidity in the market to accommodate significant increases in selling activity or the sale of a large block of our securities. Our ADSs have historically had limited trading volume, which may also result in volatility. If any of our large investors,

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such as the participants in our October 2009 private placement, seek to sell substantial amounts of our ADSs, particularly if these sales are in a rapid or disorderly manner, or other investors perceive that these sales could occur, the market price of our ADSs could decrease significantly.

The market price of our ADSs and common shares may also be affected by factors such as:



period-to-period variations in our results of operations.

Actual or potential sales of our common shares by our employees, including members of our senior management team, pursuant to pre-arranged stock trading plans could cause our stock price to fall or prevent it from increasing for numerous reasons, and actual or potential sales by such persons could be viewed negatively by other investors.

In accordance with the guidelines specified under Rule 10b5-1 of the Securities and Exchange Act of 1934 and our policies regarding stock transactions, a number of our directors and employees, including members of our senior management team, have adopted and may continue to adopt pre-arranged stock trading plans to sell a portion of our common stock. Generally, sales under such plans by members of our senior management team and directors require public filings. Actual or potential sales of our ADSs by such persons could cause the price of our ADSs to fall or prevent it from increasing for numerous reasons. For example, a substantial amount of our ADSs becoming available (or being perceived to become available) for sale in the public market could cause the market price of our ADSs to fall or prevent it from increasing. Also, actual or potential sales by such persons could be viewed negatively by other investors.

We may be a passive foreign investment company, or PFIC, which would result in adverse U.S. federal tax consequences to U.S. investors.

Amarin Corporation plc and certain of our subsidiaries may be classified as passive foreign investment companies, or PFICs, for U.S. federal income tax purposes. The tests for determining PFIC status for a taxable year depend upon the relative values of certain categories of assets and the relative amounts of certain kinds of income. The application of these factors depends upon our financial results, which are beyond our ability to predict or control, and which may be subject to legal and factual uncertainties.

We believe it prudent to assume that we were classified as a PFIC in 2012. However, it is possible that, because of the commencement of sales and marketing of Vascepa, we may not be classified as a PFIC in 2013 or in future years, although there can be no assurance in this regard.

If we are a PFIC, U.S. holders of notes, ordinary shares or ADSs would be subject to adverse U.S. federal income tax consequences, such as ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred,

and additional reporting requirements under U.S. federal income tax laws and regulations. Whether or not U.S. holders of our ADSs make a timely QEF election or mark-to-market election may affect the U.S. federal income tax consequences to U.S. holders with respect to the acquisition, ownership and disposition of Amarin ADSs and any distributions such U.S. Holders may receive.

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A QEF election and other elections that may mitigate the effect of our being classified as a PFIC are unavailable with respect to the notes. Investors should consult their own tax advisors regarding all aspects of the application of the PFIC rules to the notes, ordinary shares and ADSs.

Failure to meet our obligations under our Purchase and Sale Agreement with Biopharma could adversely affect our financial results and liquidity.

Pursuant to our December 2012 Purchase and Sale Agreement with Biopharma, we are obligated to make payments to Biopharma based on the amount of our net product sales of Vascepa and any future products based on ethyl-EPA, or covered products, subject to certain quarterly caps.

Pursuant to this agreement, we may not, among other things: (i) incur indebtedness greater than a specified amount, which we refer to as the Indebtedness Covenant; (ii) pay a dividend or other cash distribution, unless we have cash and cash equivalents in excess of a specified amount after such payment; (iii) amend or restate our memorandum and articles of association unless such amendments or restatements do not affect Biopharma s interests under the transaction; (iv) encumber any of the collateral securing our performance under the agreement; and (v) abandon certain patent rights, in each case without the consent of Biopharma.

Upon a transaction resulting in a change of control of Amarin, as defined in the agreement, Biopharma will be automatically entitled to receive any amounts not previously paid, up to our maximum repayment obligation. As defined in the agreement, change of control includes, among other things, (i) a greater than 50 percent change in the ownership of Amarin, (ii) a sale or disposition of any collateral securing our debt with Biopharma and (iii), unless Biopharma has been paid a certain amount under the indebtedness, the licensing of Vascepa to a third party for sale in the United States. The acceleration of the payment obligation in the event of a change of control transaction may make us less attractive to potential acquirers, and the payment of such funds out of our available cash or acquisition proceeds would reduce acquisition proceeds for our stockholders.

To secure our obligations under the agreement, we granted Biopharma a security interest in our rights in patents, trademarks, trade names, domain names, copyrights, know-how and regulatory approvals related to the covered products, all books and records relating to the foregoing and all proceeds of the foregoing, which we refer to as the collateral. If we (i) fail to deliver a payment when due and do not remedy that failure within specific notice period, (ii) fail to maintain a first-priority perfected security interest in the collateral in the United States and do not remedy that failure after receiving notice of such failure or (iii) become subject to an event of bankruptcy, then Biopharma may attempt to collect the maximum amount payable by us under this agreement (after deducting any payments we have already made).

There can be no assurance that we will not breach the covenants or other terms of, or that an event of default will not occur under, this agreement and, if a breach or event of default occurs, there can be no assurance that we will be able to cure the breach within the time permitted. Any failure to pay our obligations when due, any breach or default of our covenants or other obligations, or any other event that causes an acceleration of payment at a time when we do not have sufficient resources to meet these obligations, could have a material adverse effect on our business, results of operations, financial condition and future viability.

### Our existing indebtedness could adversely affect our financial condition.

Our existing indebtedness, which we entered into in January 2012, consists of \$150.0 million in aggregate principal amount of 3.50% exchangeable senior notes due 2032, with provisions for the notes to be called on or after January 19, 2017. Our indebtedness and the related annual debt service requirements may adversely impact our business, operations and financial condition in the future. For example, they could:

increase our vulnerability to general adverse economic and industry conditions;

limit our ability to raise additional funds by borrowing or engaging in equity sales in order to fund future working capital, capital expenditures, research and development and other general corporate requirements;

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require us to dedicate a substantial portion of our cash to service payments on our debt; or

limit our flexibility to react to changes in our business and the industry in which we operate or to pursue certain strategic opportunities that may present themselves.

The accounting method for convertible debt securities that may be settled in cash, such as our notes, could have a material effect on our reported financial results.

Under the FASB Accounting Standards Codification, or ASC, we may be required to separately account for the liability and equity components of the convertible debt instruments (such as the notes) that may be settled entirely or partially in cash upon conversion in a manner that reflects the issuer—s economic interest cost. The effect of ASC on the accounting for our outstanding convertible notes may be that the equity component is required to be included in the additional paid-in capital section of stockholders—equity on our consolidated balance sheets and the value of the equity component would be treated as original issue discount for purposes of accounting for the debt component of the notes. As a result, we may be required to record non-cash interest expense as a result of the amortization of the discounted carrying value of the notes to their face amount over the term of the notes. We may be required to report higher interest expense in our financial results because ASC may require interest to include both the current period—s amortization of the debt discount and the instrument—s coupon interest, which could adversely affect our reported or future financial results and the trading price of our ADSs.

Servicing our debt may require a significant amount of cash, and we may not have sufficient cash flow from our business to provide the funds sufficient to pay our substantial debt.

Our ability to make scheduled payments of the principal of, to pay interest on or to refinance our indebtedness, including the notes, depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not continue to generate cash flow from operations in the future sufficient to service our debt and make necessary capital expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations, including the notes, and have a material adverse effect on the trading price of our ADSs.

We may be able to incur substantial additional debt in the future, subject to the restrictions contained in our future debt instruments, if any, which would intensify the risks discussed above.

The conditional exchange feature of the notes, if triggered, may adversely affect our financial condition and operating results.

In the event the conditional exchange feature of the notes is triggered, holders of notes will be entitled to exchange the notes at any time during specified periods at their option. If one or more holders elect to exchange their notes, unless we elect to satisfy its exchange obligation by delivering solely the ADSs (other than cash in lieu of any fractional ADS), we would be required to settle a portion or all of its exchange obligation through the payment of cash, which could adversely affect our liquidity. In addition, even if holders do not elect to exchange their notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the notes as a current rather than long-term liability, which would result in a material reduction of our net working capital.

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### The fundamental change repurchase feature of the notes may delay or prevent an otherwise beneficial takeover attempt of us.

The indenture governing the notes will require us to repurchase the notes for cash upon the occurrence of a fundamental change of Amarin and, in certain circumstances, to increase the exchange rate for a holder that exchanges its notes in connection with a make-whole fundamental change. A takeover of us may trigger the requirement that we purchase the notes and/or increase the exchange rate, which could make it more costly for a potential acquirer to engage in a combinatory transaction with us. Such additional costs may have the effect of delaying or preventing a takeover of us that would otherwise be beneficial to investors.

#### We do not intend to pay cash dividends on the ordinary shares in the foreseeable future.

We have never paid dividends on ordinary shares and do not anticipate paying any cash dividends on the ordinary shares in the foreseeable future. Under English law, any payment of dividends would be subject to relevant legislation and our Articles of Association, which requires that all dividends must be approved by our Board of Directors and, in some cases, our shareholders, and may only be paid from our distributable profits available for the purpose, determined on an unconsolidated basis.

### The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation.

We are incorporated under English law. The rights of holders of ordinary shares and, therefore, certain of the rights of holders of ADSs, are governed by English law, including the provisions of the Companies Act 2006, and by our Articles of Association. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations. The principal differences include the following:

Under English law and our Articles of Association, each shareholder present at a meeting has only one vote unless demand is made for a vote on a poll, in which case each holder gets one vote per share owned. Under U.S. law, each shareholder typically is entitled to one vote per share at all meetings. Under English law, it is only on a poll that the number of shares determines the number of votes a holder may cast. You should be aware, however, that the voting rights of ADSs are also governed by the provisions of a deposit agreement with our depositary bank.

Under English law, subject to certain exceptions and disapplications, each shareholder generally has preemptive rights to subscribe on a proportionate basis to any issuance of ordinary shares or rights to subscribe for, or to convert securities into, ordinary shares for cash. Under U.S. law, shareholders generally do not have preemptive rights unless specifically granted in the certificate of incorporation or otherwise.

Under English law and our Articles of Association, certain matters require the approval of 75% of the shareholders who vote (in person or by proxy) on the relevant resolution (or on a poll shareholders representing 75% of the ordinary shares voting (in person or by proxy)), including amendments to the Articles of Association. This may make it more difficult for us to complete corporate transactions deemed advisable by our board of directors. Under U.S. law, generally only majority shareholder approval is required to amend the certificate of incorporation or to approve other significant transactions.

In the United Kingdom, takeovers may be structured as takeover offers or as schemes of arrangement. Under English law, a bidder seeking to acquire us by means of a takeover offer would need to make an offer for all of our outstanding ordinary shares/ADSs. If acceptances are not received for 90% or more of the ordinary shares/ADSs under the offer, under English law, the bidder cannot complete a squeeze out to obtain 100% control of us. Accordingly, acceptances of 90% of our outstanding ordinary shares/ADSs will likely be a condition in any takeover offer to acquire us, not 50% as is more common in tender offers for corporations organized under Delaware law. By contrast, a scheme of arrangement, the successful completion of which would result in a bidder obtaining 100% control of us, requires the

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approval of a majority of shareholders voting at the meeting and representing 75% of the ordinary shares voting for approval.

Under English law and our Articles of Association, shareholders and other persons whom we know or have reasonable cause to believe are, or have been, interested in our shares may be required to disclose information regarding their interests in our shares upon our request, and the failure to provide the required information could result in the loss or restriction of rights attaching to the shares, including prohibitions on certain transfers of the shares, withholding of dividends and loss of voting rights. Comparable provisions generally do not exist under U.S. law.

The quorum requirement for a shareholders—meeting is a minimum of two shareholders entitled to vote at the meeting and present in person or by proxy or, in the case of a shareholder which is a corporation, represented by a duly authorized officer. Under U.S. law, a majority of the shares eligible to vote must generally be present (in person or by proxy) at a shareholders—meeting in order to constitute a quorum. The minimum number of shares required for a quorum can be reduced pursuant to a provision in a company—s certificate of incorporation or bylaws, but typically not below one-third of the shares entitled to vote at the meeting.

### U.S. shareholders may not be able to enforce civil liabilities against us.

We are incorporated under the laws of England and Wales, and our subsidiaries are incorporated in various jurisdictions, including foreign jurisdictions. A number of the officers and directors of each of our subsidiaries are non-residents of the United States, and all or a substantial portion of the assets of such persons are located outside the United States. As a result, it may not be possible for investors to affect service of process within the United States upon such persons or to enforce against them judgments obtained in U.S. courts predicated upon the civil liability provisions of the federal securities laws of the United States. We have been advised by our English solicitors that there is doubt as to the enforceability in England in original actions, or in actions for enforcement of judgments of U.S. courts, of civil liabilities to the extent predicated upon the federal securities laws of the United States.

Our directors, management and affiliated investment funds exercise significant control over our company, which will limit your ability to influence corporate matters.

As of June 30, 2013 our executive officers, directors and affiliated investment funds collectively controlled approximately 10.2% of our outstanding ordinary shares, excluding any shares subject to ADSs that such persons may have the right to acquire upon exercise of outstanding options or warrants. As a result, these shareholders, if they act together, will be able to influence our management and affairs and all matters requiring shareholder approval, including the election of directors and approval of significant corporate transactions.

In addition, we entered into an agreement with various participants in the October 2009 private placement under which investment funds affiliated with Orbimed Advisors LLC, Sofinnova Ventures and Abingworth LLP have the ability to designate persons for Amarin to nominate to its Board of Directors and the other participants have given these investments funds a proxy to vote their securities in favor of these nominees. We have a continuing obligation to nominate one (1) designee of investment funds affiliated with Sofinnova Ventures to its Board of Directors for so long as such funds beneficially own at least fifty percent (50%) of the ADSs they purchased in the October 2009 private placement. Dr. James I. Healy was designated by investment funds affiliated with Sofinnova Ventures pursuant to this arrangement. In addition, we have agreed to nominate one (1) designee of investment funds affiliated with Abingworth LLP to its Board of Directors for so long as such funds beneficially own at least five percent (5%) of our outstanding voting securities. Dr. Joseph Anderson was designated by investment funds affiliated with Abingworth LLP under this arrangement. Dr. Anderson has resigned from the Board of Directors effective at our 2013 Annual General Meeting of Shareholders, to be held in July 2013. This concentration of ownership and the above-described arrangement may have the effect of delaying or preventing a change in control of our company that other shareholders may desire and might negatively affect the market price of the ADSs.

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U.S. holders of the ADSs or ordinary shares may be subject to U.S. federal income taxation at ordinary income tax rates on undistributed earnings and profits.

There is a risk that we will be classified as a controlled foreign corporation, or CFC, for U.S. federal income tax purposes. If we are classified as a CFC, any ADS holder or shareholder that is a U.S. person that owns directly, indirectly or by attribution, 10% or more of the voting power of our outstanding shares may be subject to U.S. income taxation at ordinary income tax rates on all or a portion of our undistributed earnings and profits attributable to subpart F income. Such 10% holder may also be taxable at ordinary income tax rates on any gain realized on a sale of ordinary shares or ADS, to the extent of our current and accumulated earnings and profits attributable to such shares. The CFC rules are complex and U.S. Holders of the ordinary shares or ADSs are urged to consult their own tax advisors regarding the possible application of the CFC rules to them in their particular circumstances.

#### Risks Related to this Offering

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

We have not designated the amount of net proceeds we will use for any particular purpose. Accordingly, our management will have broad discretion as to the application of the net proceeds and could use them for purposes other than those contemplated at the time of this offering. Our shareholders may not agree with the manner in which our management chooses to allocate and spend the net proceeds. Moreover, our management may use the net proceeds for corporate purposes that may not increase our profitability or our market value. See Use of Proceeds for a description of our management s intended use of the proceeds from this offering.

You will experience immediate dilution in the book value per share of the ADSs you purchase.

Because the price per share of our ADSs being offered is substantially higher than the book value per share of our ADSs, you will suffer substantial dilution in the net tangible book value of the ADSs you purchase in this offering. Based on the public offering price of \$ per ADS, if you purchase ADSs in this offering, you will suffer immediate and substantial dilution of \$ per ADS compared to the net tangible book value of the ADSs as of March 31, 2013. To the extent outstanding options and warrants are exercised, you will experience significant additional dilution. See Dilution for a more detailed discussion of the dilution you will incur in this offering.

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#### SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein contain express or implied forward-looking statements. Forward-looking statements relate to future events or our future financial performance. We generally identify forward-looking statements by terminology such as may, will, would, should, expects, plans, anticipates, could. intends. contemplates, believes, estimates, predicts, assume, intend, potential, continue or other similar words or the negative of these terms statements are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. The outcome of the events described in these forward-looking statements is subject to risks, uncertainties and other factors described in Risk Factors and in our periodic filings with the SEC, incorporated by reference or included in this prospectus supplement and the accompanying prospectus. Accordingly, you should not place undue reliance upon these forward-looking statements. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur, the timing of events and circumstances and actual results could differ materially from those projected in the forward-looking statements. Forward-looking statements contained herein include, but are not

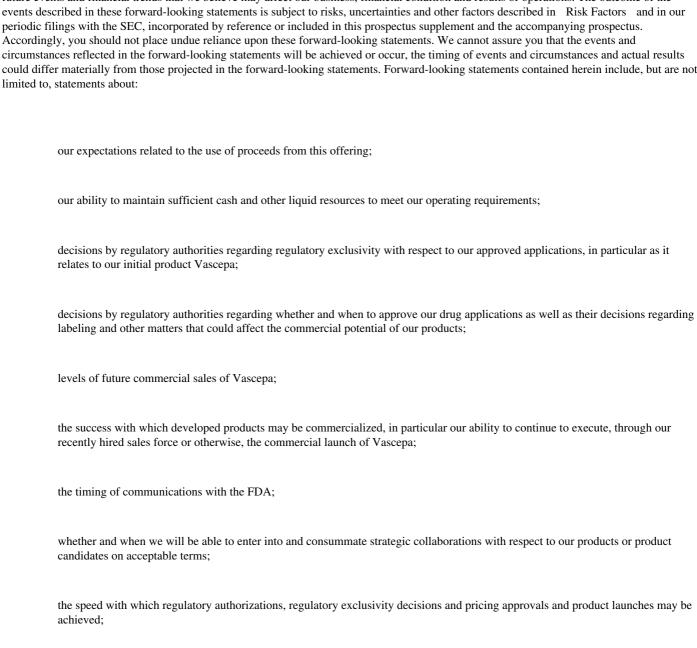


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the success of our research and development activities;

the safety and efficacy of our products and product candidates;

the propensity of clinicians to prescribe our products to approved patient populations;

estimates of the potential markets for our products and product candidates;

our expectations reading the qualification of additional third party manufacturing suppliers and estimates of the capacity of manufacturing and other facilities to support our products;

competitive developments affecting our products or product candidates, including generic and branded competition;

the scope of our intellectual property protection and the likelihood of securing additional patent protection;

our ability to protect our patents and other intellectual property;

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the effect of possible domestic and foreign legislation or regulatory action affecting, among other things, pharmaceutical pricing and reimbursement, including under Medicaid and Medicare in the United States, and involuntary approval of prescription medicines for over-the-counter use and the trend toward managed care and health care cost containment;

claims and concerns that may arise regarding the safety or efficacy of our products or product candidates;

governmental laws and regulations affecting our operations, including those affecting taxation; and

growth in costs and expenses.

The forward-looking statements made or incorporated by reference herein relate only to events as of the date on which the statements are made. We have included important factors in the cautionary statements included herein and incorporated herein by reference, including under the caption entitled Risk Factors that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. Except as required by law, we do not assume any intent to update any forward-looking statements after the date on which the statement is made, whether as a result of new information, future events or circumstances or otherwise.

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#### DESCRIPTION OF AMERICAN DEPOSITARY SHARES

Citibank, N.A. has agreed to act as the depositary bank for the American Depositary Shares. Citibank s depositary offices are located at 388 Greenwich Street, New York, New York 10013. American Depositary Shares are frequently referred to as ADSs and represent ownership interests in securities that are on deposit with the depositary bank. ADSs may be represented by certificates that are commonly known as American Depositary Receipts or ADRs. The depositary bank typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank, N.A., London Branch, having its principal office at Citigroup Centre, Canada Square, Canary Wharf, London E14 5LB, England.

We have appointed Citibank as depositary bank pursuant to an amended and restated as of November 4, 2011. A copy of the deposit agreement is on file with the SEC under cover of a Registration Statement on Form F-6 filed on September 16, 2011. You may obtain a copy of the deposit agreement from the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and from the SEC s website (www.sec.gov). Please refer to Registration Number 333-176898 when retrieving such copy.

We are providing you with a summary description of the material terms of the ADSs and of your material rights as an owner of ADSs. Please remember that summaries by their nature lack the precision of the information summarized and that the rights and obligations of an owner of ADSs will be determined by reference to the terms of the deposit agreement and not by this summary. We urge you to review the deposit agreement in its entirety.

Each ADS represents the right to receive one ordinary share on deposit with the custodian. An ADS also represents the right to receive any other property received by the depositary bank or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. The custodian, the depositary bank and their respective nominees will hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depositary bank, the custodian or their nominees. Beneficial ownership in the deposited property will under the terms of the deposit agreement be vested in the beneficial owners of the ADSs. The depositary bank, the custodian and their respective nominees will be the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. Owners of ADSs will be able to exercise beneficial ownership interests in the deposited property only through the registered holders of the ADSs, by the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depositary bank, and by the depositary bank (on behalf of the owners of the corresponding ADSs) directly, or indirectly through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.

If you become an owner of ADSs, you will become a party to the deposit agreement and therefore will be bound to its terms and to the terms of any ADR that represents your ADSs. The deposit agreement and the ADR specify our rights and obligations as well as your rights and obligations as owner of ADSs and those of the depositary bank. As an ADS holder you appoint the depositary bank to act on your behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of ordinary shares will continue to be governed by the laws of England and Wales, which may be different from the laws in the United States.

As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depositary bank in your name reflecting the registration of uncertificated ADSs directly on the books of the depositary bank (commonly referred to as the direct registration system or DRS). The direct registration system reflects the uncertificated (book-entry) registration of ownership of ADSs by the depositary bank. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depositary bank to the holders of the