

AMARIN CORP PLC\UK
Form 10-K
February 27, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2018

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF
1934

For the transition period from to

Commission File No. 0-21392

Amarin Corporation plc

(Exact name of registrant as specified in its charter)

England and Wales Not applicable
(State or other jurisdiction of (I.R.S. Employer

incorporation or organization) Identification No.)

2 Pembroke House

Upper Pembroke Street 28-32, Dublin 2, Ireland

(Address of principal executive offices)

Edgar Filing: AMARIN CORP PLC\UK - Form 10-K

+353 (0) 1 6699 020

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
---------------------	---

American Depositary Shares, each representing one Ordinary Share	
--	--

Ordinary Shares, 50 pence par value per share	The NASDAQ Stock Market LLC
---	-----------------------------

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES NO

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. YES NO

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES NO

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). YES NO

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company
Emerging growth company	

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES NO

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2018 was approximately \$902.0 million, based upon the closing price on the NASDAQ Capital Market reported for such date.

329,321,488 shares were outstanding as of February 22, 2019, including 329,087,415 shares held as American Depositary Shares (ADSs), each representing one Ordinary Share, 50 pence par value per share and 234,073 Ordinary Shares. In addition, 28,931,746 ordinary share equivalents were issuable in exchange for outstanding preferred shares as of February 22, 2019, for a total of 358,253,234 ordinary shares and ordinary share equivalents outstanding as of February 22, 2019.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required to be disclosed in Part III of this report is incorporated by reference from the registrant's definitive proxy statement to be filed not later than 120 days after the end of the fiscal year covered by this report.

Table of Contents

	Page
<u>PART I</u>	
Item 1. <u>Business</u>	1
Item 1A. <u>Risk Factors</u>	27
Item 1B. <u>Unresolved Staff Comments</u>	63
Item 2. <u>Properties</u>	63
Item 3. <u>Legal Proceedings</u>	64
Item 4. <u>Mine Safety Disclosures</u>	65
<u>PART II</u>	
Item 5. <u>Market For Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	66
Item 6. <u>Selected Financial Data</u>	70
Item 7. <u>Management’s Discussion and Analysis of Financial Condition and Results of Operations</u>	71
Item 7A. <u>Quantitative and Qualitative Disclosures about Market Risk</u>	87
Item 8. <u>Financial Statements and Supplementary Data</u>	88
Item 9. <u>Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	88
Item 9A. <u>Controls and Procedures</u>	88
Item 9B. <u>Other Information</u>	91
<u>PART III</u>	
Item 10. <u>Directors, Executive Officers and Corporate Governance</u>	
Item 11. <u>Executive Compensation</u>	92
Item 12. <u>Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	92
Item 13. <u>Certain Relationships and Related Transactions, and Director Independence</u>	92
Item 14. <u>Principal Accountant Fees and Services</u>	92
<u>PART IV</u>	
Item 15. <u>Exhibits and Financial Statement Schedules</u>	93
Item 16. <u>Form 10-K Summary</u>	99
<u>SIGNATURES</u>	100

PART I

SPECIAL NOTE REGARDING

FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical fact contained in this Annual Report on Form 10-K are forward-looking statements, including statements regarding the progress and timing of our clinical programs, regulatory filings and commercialization activities, and the potential clinical benefits, safety and market potential of our product candidates, as well as more general statements regarding our expectations for future financial and operational performance, regulatory environment, and market trends. In some cases, you can identify forward-looking statements by terminology such as “may,” “would,” “should,” “could,” “expects,” “aims,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “projects,” “potential,” or “continue”; the negative terms; or other comparable terminology. These statements include but are not limited to statements regarding the commercial success of Vascepa and factors that can affect such success; interpretation of court decisions; expectation on determinations and policy positions of the United States Food and Drug Administration, or FDA; the expected timing of enrollment, interim results and final results of our REDUCE-IT study; the safety and efficacy of our product and product candidates; expectation regarding the potential for Vascepa to be partnered, developed and commercialized outside of the United States; expectation on the scope and strength of our intellectual property protection and the likelihood of securing additional patent protection; estimates of the potential markets for our product candidates; estimates of the capacity of manufacturing and other facilities to support our products; our operating and growth strategies; our industry; our projected cash needs, liquidity and capital resources; and our expected future revenues, operations and expenditures.

Forward-looking statements are only current predictions and are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry’s actual results, levels of activity, performance, or achievements to be materially different from those anticipated by such statements. These factors include, among other things, those listed under “Risk Factors” in Item 1A of Part I of this Annual Report on Form 10-K and elsewhere in this Annual Report on Form 10-K. These and other factors could cause results to differ materially from those expressed in these forward-looking statements.

Although we believe that the expectations reflected in the forward-looking statements contained in this Annual Report on Form 10-K are reasonable, we cannot guarantee future results, performance, or achievements. Except as required by law, we are under no duty to update or revise any of such forward-looking statements, whether as a result of new information, future events or otherwise, after the date of this Annual Report on Form 10-K.

Unless otherwise indicated, information contained in this Annual Report on Form 10-K concerning our product candidates, the number of patients that may benefit from these product candidates and the potential commercial opportunity for our product candidates, is based on information from independent industry analysts and third-party sources (including industry publications, surveys, and forecasts), our internal research, and management estimates. Management estimates are derived from publicly available information released by independent industry analysts and third-party sources, as well as data from our internal research, and based on assumptions made by us based on such data and our knowledge of such industry, which we believe to be reasonable. None of the sources cited in this Annual Report on Form 10-K has consented to the inclusion of any data from its reports, nor have we sought their consent. Our internal research has not been verified by any independent source, and we have not independently verified any third-party information. While we believe that such information included in this Annual Report on Form 10-K is generally reliable, such information is inherently imprecise. In addition, projections, assumptions, and estimates of our future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in “Risk Factors” in Item 1A of Part I of this Annual Report on Form 10-K and elsewhere in

this Annual Report on Form 10-K. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

Item 1. Business

References in this report to “Amarin,” the “Company,” “we,” “our” and “us” refer to Amarin Corporation plc and its subsidiaries on a consolidated basis, unless otherwise indicated.

This Annual Report on Form 10-K includes the registered and unregistered trademarks and service marks of other parties.

Amarin Corporation plc is a public limited company incorporated under the laws of England and Wales. Amarin Corporation plc 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 principal offices are located at 2 Pembroke House, Upper Pembroke Street 28-32, Dublin 2 Ireland. Our registered office is located at One New Change, London EC4M 9AF, England. Our primary office in the United States is located at 1430 Route 206, Bedminster, NJ 07921, USA. Our telephone number at that location is (908) 719-1315.

For purposes of this Annual Report on Form 10-K, our ordinary shares may also be referred to as “common shares” or “common stock.”

Overview

We are a pharmaceutical company with expertise in omega-3 fatty acids and lipid science focused on the commercialization and development of therapeutics to improve cardiovascular, or CV, health.

Our lead product, Vascepa® (icosapent ethyl) capsules, is approved by the U.S. Food and Drug Administration, or FDA, for use as an adjunct to diet to reduce triglyceride, or TG, levels in adult patients with severe ($TG \geq 500$ mg/dL) hypertriglyceridemia. Triglycerides are the main constituent of body fat in humans. Hypertriglyceridemia refers to a condition in which patients have high levels of triglycerides in the bloodstream. The primary targeted clinical benefit of lowering triglycerides in adult patients with severe ($TG \geq 500$ mg/dL) hypertriglyceridemia is to reduce the risk of pancreatitis. In January 2013, we began selling and marketing Vascepa in the United States based on the FDA-approved MARINE indication of patients with severely high ($TG \geq 500$ mg/dL) triglyceride levels, a patient population of approximately 4 million people in the United States.

Our FDA-approved indication for Vascepa, known as the MARINE indication, is based primarily on the successful results from the MARINE study of Vascepa in the approved patient population. In considering this approval, the FDA also reviewed the successful results from our study of Vascepa in patients with high triglyceride levels ($TG \geq 200$ mg/dL and < 500 mg/dL) who are also on statin therapy for elevated low-density lipoprotein cholesterol, or LDL-C, levels which condition we refer to as mixed dyslipidemia or persistent high triglycerides. This study is known as the ANCHOR study.

In August 2015, in addition to our FDA-approved indication, we began promoting Vascepa to healthcare professionals, or HCPs, in the United States for the lowering of triglyceride levels and other lipid and lipoprotein parameters in treatment of the patient population studied in the ANCHOR study (persistent high triglycerides after statin therapy). It is estimated that one in four adults in the United States, or more than 50 million people, have elevated (> 150 mg/dL) triglyceride levels. We also educated HCPs with supportive but not conclusive early stage and Japanese cardiovascular outcomes trial research on how the unique active ingredient in Vascepa, icosapent ethyl, might reduce the risk of coronary heart disease. This HCP promotion was based on an August 2015 federal court declaration and subsequent settlement with the FDA and U.S. government that we believe permits such promotion under the freedom of speech clause of the First Amendment to the United States Constitution. To remain truthful and non-misleading, as part of this promotion we educated HCPs on the continued uncertainty between lowering triglycerides and cardiovascular risk reduction based on the failure of other drugs (fenofibrate and formulations of niacin) to demonstrate incremental cardiovascular benefit from adding a second lipid-altering drug on top of standard of care statin therapy, despite such drugs reducing triglyceride levels and having other favorable effects on lipid and lipoprotein parameters. We believe that, in general, HCPs prefer to review and rely on robust cardiovascular outcomes trial results before changing prescribing practices.

Multiple primary and secondary prevention trials have shown a significant relative risk reduction, or RRR, of 25% to 35% in the risk of cardiovascular events with statin therapy, leaving significant persistent residual risk despite the achievement of target LDL-C levels. Worldwide, cardiovascular disease, or CVD, remains the number one killer of men and women. In the United States, CVD leads to one in every three deaths—one death approximately every 38 seconds—with annual treatment cost in excess of \$500 billion. There is no FDA-approved therapy for lowering cardiovascular risk beyond therapies which target lowering of LDL-C levels.

Since our inception, we have devoted substantial resources to our research and development efforts, most significantly our Vascepa cardiovascular outcomes trial, REDUCE-IT™, which we commenced in 2011 and was conducted based on

a special protocol assessment, or SPA, agreement with the FDA. REDUCE-IT was a global study of 8,179 statin-treated adults with elevated cardiovascular risk. We announced topline results from the REDUCE-IT study on September 24, 2018. On November 10, 2018, we announced the more detailed, primary results from the REDUCE-IT study at the 2018 Scientific Sessions of the American Heart Association, or AHA, and the results were concurrently published in The New England Journal of Medicine. REDUCE-IT met its primary endpoint demonstrating a 25% relative risk reduction, or RRR, to a high degree of statistical significance ($p < 0.001$), in first occurrence of major adverse cardiovascular events, or MACE, in the intent-to-treat patient population with use of Vascepa 4 grams/day as compared to placebo. Patients who were enrolled in REDUCE-IT needed to have LDL-C between 41-100 mg/dL (median baseline LDL-C 75 mg/dL) controlled by statin therapy and various cardiovascular risk factors including persistent elevated triglycerides, or TG, between 135-499 mg/dL (median baseline 216 mg/dL) and either established cardiovascular disease (secondary prevention cohort) or be at least age 50 with diabetes mellitus and at least one other CV risk factor (primary prevention cohort). Approximately 59% of the patients had diabetes at baseline, approximately 71% of the patients had established cardiovascular disease at time of enrollment and approximately 29% were primary prevention subjects at high risk for cardiovascular disease. REDUCE-IT also showed a 26% RRR in its key secondary composite endpoint of cardiovascular death, heart attacks and stroke ($p < 0.001$).

In September 2018, in connection with the public release of topline REDUCE-IT results, we commenced communications to healthcare professionals which were intended to ensure we meet our continuing obligation to update HCPs regarding off-label use of

Vascepa to ensure that our communications remain truthful and non-misleading. We believe this promotion is consistent with the federal court approved settlement with the FDA and U.S. government. After publication of primary results of the REDUCE-IT study in The New England Journal of Medicine and the scientific presentation of REDUCE-IT results at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018, we updated and expanded our communication of REDUCE-IT results to include the publication and the peer-reviewed information presented in an effort to further ensure that our communications remain truthful and non-misleading. While we believe we are now permitted under the settlement and our First Amendment rights to more broadly promote Vascepa, the FDA-approved labeling for Vascepa has not changed as we have not yet applied for FDA approval for marketing claims related to REDUCE-IT. Also, neither government nor other third-party coverage or reimbursement to pay for the off-label use of Vascepa promoted was covered under the court declaration or settlement. We plan to submit a supplemental new drug application, or sNDA, to the FDA seeking revised labeling for Vascepa based on results of the REDUCE-IT study and, upon such expanded labeling, subject to FDA approval of such label, to further expand its promotion of Vascepa in the United States.

We sell Vascepa principally to a limited number of major wholesalers, as well as selected regional wholesalers and specialty pharmacy providers, or collectively, our Distributors or our customers, that in turn resell Vascepa to retail pharmacies for subsequent resale to patients and healthcare providers. We market Vascepa in the United States through our direct sales force. In March 2014, we entered into a co-promotion agreement in the United States with Kowa Pharmaceuticals America, Inc. under which Kowa Pharmaceuticals America, Inc. began to co-promote Vascepa in conjunction with its promotion of its primary product, a branded statin for patients with high cholesterol, which commenced in May 2014 and extended until the end of 2018. Amarin and Kowa Pharmaceuticals America, Inc. intentionally designed the co-promotion to naturally end as of December 31, 2018 and mutually agreed not to renew the agreement. Prior to the REDUCE-IT results topline announcement in September 2018, our direct sales force consisted of approximately 170 sales professionals, including sales representatives and their managers. We have recently increased the size of our sales force to approximately 440 sales professionals, including approximately 400 sales representatives, in the United States pursuant to positive REDUCE-IT results and are expanding our promotion of Vascepa. Such promotion, prior to results of the REDUCE-IT study, was based on demonstrated changes in biomarkers based on our MARINE and ANCHOR studies. Most healthcare professionals express that they prefer outcomes data to biomarker data. Because prior to results of the REDUCE-IT study we did not have outcomes data regarding the clinical effect of Vascepa and because a substantial portion of our resources were being spent on the REDUCE-IT study, prior to REDUCE-IT results our commercialization of Vascepa was somewhat limited. Subsequent to learning the positive cardiovascular outcomes results of the REDUCE-IT study, we have begun increasing our promotion of Vascepa.

In addition to promotion of Vascepa in the United States, we have entered into strategic partnerships and license arrangements in Asia, the Middle East, North Africa and Canada to further promote, develop and commercialize Vascepa. In February 2015, we entered into an exclusive agreement with Eddingpharm (Asia) Macao Commercial Offshore Limited, or Eddingpharm, to develop and commercialize Vascepa capsules in Mainland China, Hong Kong, Macau and Taiwan, or the China Territory. In March 2016, we entered into an agreement with Biologix FZCo, or Biologix, to register and commercialize Vascepa in countries within the Middle East and North Africa. In September 2017, we entered into an agreement with HLS Therapeutics Inc., or HLS, to register, commercialize and distribute Vascepa in Canada.

In June 2018, we entered into a collaboration with Mochida Pharmaceutical Co., Ltd., or Mochida, related to development and potential subsequent commercialization of drug products and indications based on the active pharmaceutical ingredient in Vascepa, the omega-3 acid, EPA (icosapentaenoic acid). The potential new product and indication opportunities contemplated under this agreement are currently in early stages of development.

We continue to assess other collaboration opportunities to maximize the value of the Vascepa franchise globally.

Commercialization—United States

We commenced the commercial launch of 1-gram size Vascepa capsules in the United States in January 2013. We commenced sales and shipments of Vascepa at that time to our network of U.S.-based wholesalers. Prior to the REDUCE-IT results topline announcement in September 2018, our direct sales force consisted of approximately 170 sales professionals, including sales representatives and their managers. We have recently increased the size of our sales force to approximately 440 sales professionals, including approximately 400 sales representatives, pursuant to positive REDUCE-IT results and are expanding our promotion of Vascepa. Commencing in May 2014, in addition to Vascepa promotion by our sales representatives, Kowa Pharmaceuticals America, Inc. began co-promoting Vascepa in conjunction with its promotion of its primary product, a branded statin for patients with high cholesterol. Amarin and Kowa Pharmaceuticals America, Inc. intentionally designed the co-promotion to naturally end as of December 31, 2018 and mutually agreed not to renew the agreement. We also employ various medical affairs and marketing personnel to support our commercialization of Vascepa. We expanded certain medical education and market awareness initiatives following the reporting of positive REDUCE-IT results in 2018. We intend to further expand promotion of Vascepa following label expansion of Vascepa, subject to FDA approval of such expanded label.

In October 2016, in addition to the original 1-gram capsule size for Vascepa, we introduced a smaller 0.5-gram capsule size, the first and only 0.5-gram prescription omega-3 alternative available on the market, for the subset of patients who prefer a smaller capsule. The FDA-approved dosing for Vascepa continues to be 4 grams per day, and, as expected, the majority of new and existing patients taking Vascepa continue to be prescribed the 1-gram size Vascepa capsule.

From May 2014 until December 2018, under our co-promotion agreement with Kowa Pharmaceuticals America, Inc., both parties agreed to use commercially reasonable efforts to promote, detail and optimize sales of Vascepa in the United States and agreed to specific performance requirements detailed in the related agreement. The performance requirements included a negotiated minimum number of sales details to be delivered by each party in the first and second position, the use of a negotiated number of minimum sales representatives from each party, and the achievement of minimum levels of Vascepa revenue in 2015 and beyond. First position referred to when a sales representative's primary purpose in detailing is related to Vascepa, while second position referred to when a sales representative's primary purpose in detailing is to promote another product, but they also devoted time in the same sales call to promote Vascepa. Kowa Pharmaceuticals America, Inc. also agreed to bear the costs incurred for its sales force associated with the commercialization of Vascepa and to pay for certain incremental costs associated with the use of its sales force, such as sample costs and costs for promotional and marketing materials. We recognized all revenue from sales of Vascepa. In exchange for Kowa Pharmaceuticals America, Inc.'s co-promotional services, Kowa Pharmaceuticals America, Inc. was entitled to a quarterly co-promotion fee based on a percentage of aggregate Vascepa gross margin that varied during the term. The percentage of aggregate Vascepa gross margin earned by Kowa Pharmaceuticals America, Inc. was, as amended, approximately eighteen percent (18%) in 2017, partially offset by certain other refinements. During 2018, which was the last year of the agreement, as amended, we incurred expense for both the annual co-promotion fee, which in 2018 was calculated as eighteen-and-a-half percent (18.5%) of Vascepa gross margin, plus accrual for co-promotion tail payments which are calculated as a percentage of the 2018 co-promotion fee. Kowa Pharmaceuticals America, Inc. is eligible to receive \$17.8 million in co-promotion tail payments, the present value of which of \$16.6 million was fully accrued as of December 31, 2018. The accrued tail payments will be paid over three years with declining amounts each year beginning with \$7.3 million to be paid in 2019.

Based on monthly compilations of data provided by a third party, Symphony Health, the estimated number of normalized total Vascepa prescriptions for the three months ended December 31, 2018 was approximately 539,000 compared to 458,000, 430,000, 391,000, and 404,000 in the three months ended September 30, 2018, June 30, 2018, March 31, 2018, and December 31, 2017, respectively. According to data from another third party, IQVIA, the estimated number of normalized total Vascepa prescriptions for the three months ended December 31, 2018 was approximately 538,000 compared to 457,000, 430,000, 392,000, and 409,000 in the three months ended September 30, 2018, June 30, 2018, March 31, 2018, and December 31, 2017, respectively. Normalized total prescriptions represent the estimated total number of Vascepa prescriptions dispensed to patients, calculated on a normalized basis (i.e., one month's supply, or total capsules dispensed multiplied by the number of grams per capsule divided by 120 grams). Inventory levels at wholesalers tend to fluctuate based on seasonal factors, prescription trends and other factors.

The data reported above is based on information made available to us from third-party resources and may be subject to adjustment and may overstate or understate actual prescriptions. Timing of shipments to wholesalers, as used for revenue recognition purposes, and timing of prescriptions as estimated by these third parties may differ from period to period. Although we believe this data is prepared on a period-to-period basis in a manner that is generally consistent and that such results can be generally indicative of current prescription trends, the data is based on estimates and should not be relied upon as definitive. While we expect to be able to grow Vascepa revenues over time, no guidance should be inferred from the operating metrics described above. We also anticipate that such sales growth will be inconsistent from period to period. 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, quarterly changes in Distributor purchases, and other factors. We believe investors should consider our results over several quarters, or longer, before making an assessment about potential future performance.

The commercialization of pharmaceutical products is a complex undertaking, and our ability to effectively and profitably commercialize 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.”

In August 2015, we and our co-promotion partner began communicating promotional information beyond MARINE clinical trial data to targeted healthcare professionals. Such qualified communications are being made pursuant to the August 2015 federal district court declaration and related March 2016 settlement allowing truthful and non-misleading promotion of the FDA-reviewed and agreed effects of Vascepa demonstrated in the ANCHOR clinical trial and presentation of the current state of scientific research related to the potential of Vascepa to reduce the risk of cardiovascular disease including through use of peer-reviewed scientific publications of available data.

In September 2018, in connection with the public release of topline REDUCE-IT results, we commenced communications to healthcare professionals, or HCPs, which were intended to ensure we meet our continuing obligation to update HCPs regarding off-label use of Vascepa to ensure that our communications remain truthful and non-misleading. We believe this promotion is consistent with the federal court approved settlement with the FDA and U.S. government. After publication of primary results of the REDUCE-IT study in *The New England Journal of Medicine* and the scientific presentation of REDUCE-IT results at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018, we updated and expanded our communication of REDUCE-IT results to include the publication and the peer-reviewed information presented in an effort to further ensure that our communications remain truthful and non-misleading. While we believe we are now permitted under the settlement and our First Amendment rights to more broadly promote Vascepa, the FDA-approved labeling for Vascepa has not changed as we have not yet applied for FDA approval for marketing claims related to REDUCE-IT. Also, neither government nor other third-party coverage or reimbursement to pay for the off-label use of Vascepa promoted was covered under the court declaration or settlement.

Commercialization—Outside the United States

In February 2015, we announced an exclusive agreement with Eddingpharm to develop and commercialize Vascepa capsules in what we refer to as the China Territory, consisting of the territories of Mainland China, Hong Kong, Macau and Taiwan, for uses that are currently commercialized and under development by us in the United States based on the MARINE, ANCHOR and REDUCE-IT clinical trials of Vascepa.

Under the agreement, Eddingpharm is responsible for development and commercialization activities in the China Territory and associated expenses. We will provide development assistance and be responsible for supplying the product. Terms of the agreement include up-front and milestone payments to us of up to \$169.0 million, including a non-refundable \$15.0 million up-front payment received at closing and a non-refundable milestone payment of \$1.0 million received upon successful submission of a clinical trial application, or CTA, with respect to the MARINE indication for Vascepa to the Chinese regulatory authority in March 2016. In March 2017, the CTA was approved by the Chinese regulatory authority and, in December 2017, Eddingpharm commenced a pivotal clinical trial aimed to support the regulatory approval of the first indication of Vascepa in a patient population with severe hypertriglyceridemia in Mainland China. We are also entitled to receive future regulatory and sales-based milestone payments of up to an additional \$153.0 million. The regulatory milestone events relate to the submission and approval of certain applications to the applicable regulatory authority, such as a clinical trial application, clinical trial exemption, or import drug license application. The amounts to be received upon achievement of the regulatory milestone events relate to the submission and approval for three indications, and range from \$2.0 million to \$15.0 million for a total of \$33.0 million. The sales-based milestone events occur when annual aggregate net sales of Vascepa in the territory equals or exceeds certain specified thresholds, and range from \$5.0 million to \$50.0 million for a total of \$120.0 million. Eddingpharm will also pay us tiered double-digit percentage royalties on net sales of Vascepa in the China Territory escalating to the high teens. We will supply finished product to Eddingpharm under negotiated terms.

In March 2016, we entered into an agreement with Biologix FZCo, or Biologix, to register and commercialize Vascepa in several Middle Eastern and North African countries. Under the terms of the distribution agreement, we granted to Biologix a non-exclusive license to use our trademarks in connection with the importation, distribution, promotion, marketing and sale of Vascepa in the Middle East and North Africa territory. Upon closing of the agreement, we received a non-refundable up-front payment, which will be recognized as revenue over 10 years commencing upon first marketing approval of Vascepa in the territory. We receive all payments based on total product sales and pay Biologix a service fee in exchange for its services, whereby the service fee represents a percentage of gross selling price which is subject to a minimum floor price. In March 2018 and July 2018, we received approval for Vascepa as a prescription medication for use in Lebanon and United Arab Emirates,

respectively, as an adjunct to diet to reduce triglyceride levels in adult patients with severe hypertriglyceridemia.

In September 2017, we entered into an agreement with HLS to register, commercialize and distribute Vascepa in Canada. Under the agreement, HLS will be responsible for regulatory and commercialization activities and associated costs. We will be responsible for providing assistance towards local filings, supplying finished product under negotiated supply terms, maintaining intellectual property, and continuing the development and funding of REDUCE-IT related activities. Terms of the agreement include up-front and milestone payments to us of up to \$65.0 million. These payments include a non-refundable \$5.0 million up-front payment received in two equal installments, the first of which was received at closing with the second received upon the six-month anniversary of the closing, as well as a non-refundable milestone payment of \$2.5 million received upon achievement of the REDUCE-IT trial primary endpoint. In addition to the non-refundable, up-front payment, we are entitled to receive certain regulatory and sales-based milestone payments of up to an additional \$57.5 million, the timing and achievability of which cannot be determined at this time, as well as tiered double-digit royalties on net sales of Vascepa in Canada.

We continue to assess other partnership opportunities for licensing Vascepa to partners outside of the United States.

Research and Development

Since our inception, we have devoted substantial resources to the research and development of Vascepa (icosapent ethyl) capsules. Vascepa is a single-molecule prescription product consisting of the omega-3 acid commonly known as EPA in ethyl-ester form. Vascepa is derived from fish through a stringent and complex FDA-regulated manufacturing process designed to effectively eliminate impurities and isolate and protect the single molecule active ingredient from degradation. Vascepa has been designated a new chemical entity by the FDA. Vascepa is known in scientific literature as AMR101.

Our most important clinical trials of Vascepa are summarized here and discussed in further detail below:

- The MARINE trial, a Phase 3, multi-center, placebo-controlled, randomized, double-blind, 12-week study in patients with very high (≥ 500 mg/dL) triglycerides (TG) with the primary endpoint being the lowering of TG levels;
- The ANCHOR trial, a Phase 3 multi-center, placebo-controlled, randomized, double-blind, 12-week pivotal study in patients with high (≥ 200 and < 500 mg/dL) TGs who were also receiving optimized statin therapy with the primary endpoint being the lowering of TG levels; and
 - The REDUCE-IT trial, a Phase 3 global study of 8,179 statin-treated adults with elevated cardiovascular risk with a primary endpoint being the first occurrence of major adverse cardiovascular events, or MACE, in the intent-to-treat patient population, patients with LDL-C between 41-100 mg/dL (median baseline LDL-C 75 mg/dL) controlled by statin therapy and various cardiovascular risk factors including persistent elevated TG between 135-499 mg/dL and either established cardiovascular disease (secondary prevention cohort) or age 50 or more with diabetes mellitus and at least one other CV risk factor (primary prevention cohort).

The REDUCE-IT cardiovascular outcomes study of Vascepa has been the centerpiece of our research and development efforts. Prior research on Vascepa, such as the MARINE and ANCHOR trials, had been focused on the effects of the drug on biomarkers associated with increased risk of pancreatitis and increased risk of cardiovascular events. Other prior and ongoing research and development efforts include the study of potential mechanisms of action of Vascepa.

In June 2018, we entered into a multi-faceted collaboration with Mochida related to the development and commercialization of drug products and indications based on the active pharmaceutical ingredient in Vascepa, the omega-3 acid, EPA. Among other terms in the agreement, we obtained an exclusive license to certain Mochida intellectual property to advance our interests in the United States and certain other territories and the parties will collaborate to research and develop new products and indications based on EPA for our commercialization in the United States and certain other territories. The potential new product and indication opportunities contemplated under this agreement are currently in early stages of development.

Additional research and development opportunities beyond REDUCE-IT will be assessed more fully after giving priority to securing regulatory approval for Vascepa based on the REDUCE-IT results.

Commercial and Clinical Supply

We manage the manufacturing and supply of Vascepa internally and have done so since we began clinical development of Vascepa prior to the drug's marketing approval by the FDA in 2012. We rely on contract manufacturers in each step of our commercial and clinical product supply chain. These steps include active pharmaceutical ingredient, or API, manufacturing, encapsulation of the API, product packaging and supply-related logistics. Our approach to product supply procurement is designed to mitigate risk of supply interruption and maintain an environment of cost competition through diversification of contract manufacturers at each stage of the supply chain and lack of reliance on any single supplier. We have multiple FDA-approved international API suppliers,

encapsulators and packagers to support the Vascepa commercial franchise. The amount of supply we seek to purchase in future periods will depend on the level of growth of Vascepa revenues and minimum purchase commitments with certain suppliers. While our current supply chain is scalable, we continue efforts to expand, diversify and further enhance it.

Financial Position

We believe that our cash and cash equivalents of \$249.2 million as of December 31, 2018 will be sufficient to fund our projected operations for at least twelve months and through the likely Prescription Drug User Fee Act (PDUFA) date for approval of a supplemental new drug application (sNDA) by the FDA based on REDUCE-IT study results. Depending on the level of cash generated from operations, and depending in part on the timing and results of the FDA review of the sNDA and rate of prescription growth for Vascepa, additional capital may be required to support planned expansion of Vascepa promotion and potential Vascepa promotion beyond which we are currently executing. If additional capital is required and we are unable to obtain additional capital, we may be forced to delay, limit or eliminate certain promotional activities. We anticipate that quarterly net cash outflows in future periods will be variable.

Lipid Disorders and Cardiovascular Disease

Heart attacks, strokes and other cardiovascular events represent the leading cause of death and disability among men and women in western societies. According to the Heart Disease and Stroke Statistics—2018 Update from the American Heart Association, more than 1 out of every 3 adults in the United States (approximately 92 million) currently lives with one or more types of cardiovascular disease; an estimated 1 million new or recurrent coronary events and 795,000 new or recurrent strokes occur each year; an estimated 29 million adults ≥ 20 years of age have high total serum cholesterol levels (≥ 240 mg/dL), and an estimated 71 million adults ≥ 20 years of age have borderline high or high low-density lipoprotein (“bad”) cholesterol, or LDL-C, levels (≥ 130 mg/dL).

In addition to cholesterol, lipoproteins such as LDL also carry fats in the form of triglycerides. Hypertriglyceridemia refers to a condition in which patients have high levels of triglycerides in the bloodstream and has been reported to be an independent risk factor for cardiovascular disease. Triglyceride levels provide important information as a marker associated with the risk for heart disease and stroke.

Guidelines for the management of very high triglyceride levels (≥ 500 mg/dL) suggest that reducing triglyceride levels is the primary treatment goal in these patients to reduce the risk of acute pancreatitis. Treating LDL-C remains an important secondary goal. Other important parameters to consider in patients with very high triglycerides include levels of apolipoprotein B (apo B), non-HDL-C, and very low-density lipoprotein cholesterol (VLDL-C). The effect of Vascepa on the risk for pancreatitis in patients with hypertriglyceridemia has not been determined.

It is estimated that over 25 million adults in the United States have elevated triglyceride levels ≥ 200 mg/dL and that more than 50 million adults in the United States have elevated triglyceride levels ≥ 150 mg/dL. Additionally, approximately 2 to 3 million adults in the United States have very high triglyceride levels (≥ 500 mg/dL). Since 1976, mean triglyceride levels have increased, in concert with the growing epidemic of obesity, insulin resistance, and type 2 diabetes mellitus. In contrast, mean LDL-C levels have decreased.

Mixed dyslipidemia refers to a condition in which patients have a combination of two or more lipid abnormalities including elevated triglycerides, low HDL-C, and/or elevated LDL-C. Both hypertriglyceridemia and mixed dyslipidemia are components of a range of lipid disorders collectively referred to as dyslipidemia. Dyslipidemia has been linked to atherosclerosis, commonly referred to as hardening of the arteries.

Limitations of Current Therapies

Hypertriglyceridemia (HTG) is a prevalent lipid disorder in approximately 25% of the U.S. adult population. Both epidemiological and genetic data have shown associations between HTG and coronary heart disease. Many of those patients are taking statin therapy directed at lowering the risk of CVD by lowering their LDL-C levels, primarily. Recently, real world administrative database analyses have reported an increased CVD risk as well as direct healthcare costs associated with HTG despite statin therapy and controlled LDL-C compared to those with $TG < 150$ mg/dL. It is estimated that approximately 6% or less of U.S. adults with triglyceride levels ≥ 200 mg/dL are currently receiving prescription medication for lowering triglycerides, many of whom are already on statin therapy.

Vascepa is not FDA-approved to lower TG levels in statin-treated patients with mixed dyslipidemia and persistent high (≥ 200 mg/dL and < 500 mg/dL) TG levels due to uncertainty raised by FDA in 2013 regarding the benefit, if any, of drug-induced changes in lipid/lipoprotein parameters beyond statin-lowered LDL-C on cardiovascular risk among statin-treated patients with residually high TG. This lack of approval by FDA based on the pharmaceutical target of lowering TG levels as a surrogate for lowering the risk of CVD was due primarily to the failure of cardiovascular outcomes trials of lipid altering drugs in the fenofibrate and niacin drug classes. In CV outcomes trials, therapies that reduce TG levels and had other favorable effects on classically studied lipid and lipoprotein parameters, such as

extended-release niacin and fibrates, did not meet their primary CV endpoints to reduce risk when taken with contemporary medical therapy, including statins. Specifically, cardiovascular outcomes trials, ACCORD Lipid, AIM-HIGH, and HPS2-THRIVE, while not designed to test the effect of lowering TG levels in patients with high TG levels after statin therapy, each failed to demonstrate incremental cardiovascular benefit of adding a second lipid-altering drug (fenofibrate or formulations of niacin), despite raising HDL-C and reducing TG levels, among statin-treated patients with well-controlled LDL-C. As a result, in 2015, the FDA updated both the Trilipix® (a fenofibrate) and extended-release niacin product labeling and removed combination use with statin therapy in mixed dyslipidemia patients as an indication due to a failed outcomes trial. No head-to head, randomized, well-controlled studies have been conducted to compare the effects of Vascepa with other FDA-approved TG-lowering therapies.

Additionally, recent CV outcomes trials and meta-analyses with low dose omega-3 fatty acid mixtures containing DHA have not shown substantial benefit in patients receiving contemporary medical therapy, including statins. Due to these failed low dose omega-3 CV outcomes trials, the European regulatory authorities have concluded that omega-3 fatty acid medicines (specifically Lovaza®/Omacor®) at a dose of 1-gram per day are not effective in preventing further events for patients who have had a heart attack.

It is against that backdrop of failed studies demonstrating the limitations of other add-on drugs to statin drug therapies that we conducted the REDUCE-IT cardiovascular outcomes trial.

Potential Benefits and Market Opportunity for Vascepa

Vascepa is 1-gram of icosapent ethyl, or ethyl-EPA, and contains no DHA. We believe that the removal of DHA mitigates against the LDL-C raising effect observed in omega-3 compositions that include DHA. Based on the results of the MARINE trial, Vascepa was the first omega-3 based product to demonstrate statistically significant triglyceride reduction without a statistically significant increase in LDL-C in this very high triglyceride population.

We believe that the results of the REDUCE-IT, ANCHOR and MARINE clinical trials of Vascepa and Vascepa's EPA only/DHA-free composition position Vascepa to achieve a global "best-in-class" prescription therapy in studied patient populations. Potential mechanisms of action at work in the reduction of cardiovascular events seen in REDUCE-IT as discussed in The New England Journal of Medicine publication of REDUCE-IT primary results include TG reduction, anti-thrombotic effects, antiplatelet or anticoagulant effects, membrane-stabilizing effects, effects on stabilization and/or regression of coronary plaque and inflammation reduction. Mechanisms responsible for the benefit shown in REDUCE-IT were not studied in REDUCE-IT as that was not the purpose of an outcomes study. More study is needed to determine to what extent, if any, each of these effects or others may be responsible for the CV risk reduction benefit demonstrated in REDUCE-IT.

Clinical Trials

The MARINE Trial (basis for currently FDA-approved label for Vascepa)

The MARINE trial, the largest study ever conducted with the omega-3 fatty acid ethyl EPA in treating patients with very high triglycerides (≥ 500 mg/dL), was a Phase 3, multi-center, placebo-controlled, randomized, double-blind, 12-week study. Patients were randomized into three treatment arms for treatment with Vascepa 4 gram/day, 2 gram/day or placebo. Patient enrollment in this trial began in December 2009, and enrollment and randomization was completed in August 2010 at 229 patients. The primary endpoint in the trial was the percentage change in triglyceride level from baseline compared to placebo after 12 weeks of treatment. The MARINE study primary endpoint was required to meet a stringent level of statistical significance of 1% ($p < 0.01$) in our special protocol assessment, or SPA, agreement with the FDA.

In November 2010, we reported topline data for the MARINE trial. In the trial, Vascepa met its primary endpoint at doses of 4 grams and 2 grams per day with median placebo-adjusted reductions in triglyceride levels of 33% ($p < 0.0001$) compared to placebo for 4 grams and 20% ($p = 0.0051$) compared to placebo for 2 grams. The median baseline triglyceride levels were 703 mg/dL, 680 mg/dL and 657 mg/dL for the patient groups treated with placebo, 4 grams of Vascepa and 2 grams of Vascepa, respectively.

In a pre-specified secondary analysis in the subgroup of patients with baseline triglyceride > 750 mg/dL, representing 39% of all patients, the effect of Vascepa in reducing triglyceride levels compared to placebo was 45% for 4 grams and 33% for 2 grams, both statistically significant ($p = 0.0001$ for 4 grams and $p = 0.0016$ for 2 grams, respectively). The median baseline triglyceride levels in this subgroup were 1052 mg/dL, 902 mg/dL and 948 mg/dL for placebo, 4-gram and 2-gram groups, respectively. Twenty-five percent of patients in this trial were also on background statin therapy. These patients had greater median reduction in triglyceride levels, which was also statistically significant.

Importantly, the significant reduction in triglycerides was not associated with a statistically significant increase in median LDL-C compared to placebo at either dose (-2.3% for the 4-gram group and +5.2% for the 2-gram group [both $p = NS$]). In addition, there was a statistically significant decrease in median non-HDL-C (total cholesterol less

so-called “good cholesterol”) compared to placebo with both of the Vascepa-treated groups (-18% for the 4-gram group [$p < 0.001$] and -8% for the 2-gram group [$p < 0.05$]).

The MARINE trial results also included statistically significant reductions compared to placebo in several important lipid and inflammatory biomarkers, including apo B (apolipoprotein B) (8.5%), Lp-PLA2 (lipoprotein-phospholipase A2) (13.6%), VLDL-C (very low-density lipoprotein cholesterol) (28.6%), Total Cholesterol (16.3%), and hsCRP (high-sensitivity C-reactive protein) (36.0%) at the 4-gram dose. For these achieved endpoints, p-values were <0.01 for most and <0.05 for all. Apo B (apolipoprotein B) is believed to be a sensitive biomarker of cardiovascular risk and may be a better predictor of cardiovascular risk than LDL-C. Lp-PLA2 is an enzyme found in blood and atherosclerotic plaque; high levels have been implicated in the development and progression of atherosclerosis. In a post-hoc analysis of MARINE study data, Vascepa 4 g/day and 2 g/day statistically significantly reduced ApoC-III levels by 25.1% ($p < 0.0001$) and 14.3% ($p=0.0154$) versus placebo, respectively. In the MARINE trial, patients treated with 4 grams per day of Vascepa experienced a significant reduction in median placebo-adjusted lipoprotein particle concentrations of total LDL and small LDL. When looking at lipoprotein particle concentrations and sizes as measured with nuclear magnetic resonance spectroscopy, Vascepa 4 grams per day, compared with placebo, significantly reduced median total LDL particle count by 16.3% ($p=0.0006$), which is an important factor in atherogenesis. LDL particle count and apo B are important risk markers for the prediction of cardiovascular events. Small LDL particle count, which is a common risk factor for cardiovascular events in patients with diabetes,

was reduced by 25.6% ($p < 0.0001$) compared with placebo. Vascepa 2 grams per day, compared with placebo, significantly reduced median small LDL particle count by 12.8% ($p < 0.05$) and reduced median total LDL particle count by 1.1% (NS). LDL particle size did not change significantly for the 2 or 4 gram per day doses.

Vascepa was well tolerated in the MARINE trial, with a safety profile comparable to placebo and there were no treatment-related serious adverse events observed. No patient discontinued treatment of Vascepa during this study due to Vascepa-related adverse events. No significant changes in fasting blood glucose, hemoglobin A1C, vital signs, electrocardiograms, or liver or kidney function were observed with either Vascepa dose.

Patients enrolled in the MARINE trial were given the option to be treated with Vascepa for a period of up to 40 weeks after their last dose in the double-blind portion of the trial. Once participants completed the randomized, double blind, placebo-controlled 12-week MARINE registration trial, patients in all three randomized groups (4 grams, 2 grams and placebo) were offered the opportunity to participate in the open label extension, or OLE, phase. Patients in the OLE phase received 4 grams per day of Vascepa for a period of up to an additional 40 weeks. As is typical of such extension phases, the OLE phase was not a controlled trial, as differentiated from the randomized, double blind, placebo-controlled 12-week MARINE registration trial. In the OLE phase, participants were not randomized at entry, Vascepa administration was open-label (and thus not blinded), and no placebo group was maintained. Also, once patients entered in the OLE phase, investigators were free to add or modify other lipid-altering nutritional, lifestyle and drug treatment regimens. Given the lack of randomization, the open-label design, the addition of various other lipid-altering drugs and changes to doses of existing lipid-altering drugs, as well as the lack of placebo control, neither we nor our independent advisors were able to draw efficacy conclusions from the data. However, we have concluded that the MARINE OLE phase revealed no new safety signals after an additional 40 weeks of exposure to Vascepa, whether used alone or in combination with other lipid-altering regimens.

The ANCHOR Trial (promoted in the United States under court declaration)

The ANCHOR trial was a multi-center, placebo-controlled, randomized, double-blind, 12-week pivotal study in patients with high triglycerides (≥ 200 and < 500 mg/dL) who were also receiving optimized statin therapy. Patients were randomized into three arms for treatment with Vascepa 4 gram/day, 2 gram/day or placebo. Patient enrollment in this trial began in January 2010, and enrollment and randomization was completed in February 2011 at 702 patients. The primary endpoint in the trial was the percentage change in triglyceride level from baseline compared to placebo after 12 weeks of treatment.

In April 2011, we reported topline results from the ANCHOR trial. The ANCHOR trial met its primary endpoint at doses of 4 grams and 2 grams per day with median placebo-adjusted reductions in triglyceride levels of 21.5% ($p < 0.0001$ value) for 4 grams and 10.1% ($p = 0.0005$) for 2 grams. The median baseline triglyceride levels were 259 mg/dL, 265 mg/dL and 254 mg/dL for the patient groups treated with placebo, 4 grams and 2 grams of Vascepa per day, respectively. The analysis of subgroups by baseline triglyceride tertiles showed that higher baseline triglycerides resulted in greater triglyceride reductions.

One of the trial's secondary endpoints was to demonstrate a lack of elevation in LDL-C, the primary target of cholesterol lowering therapy. The trial's non-inferiority criterion for LDL-C was met at both Vascepa doses. The upper confidence boundaries for both doses were below the pre-specified +6% LDL-C threshold limit. At the 4-gram dose the upper confidence boundary was below zero (-1.7%) and at the 2-gram dose the upper confidence boundary was close to zero (0.5%). For the 4 grams per day group, LDL-C decreased significantly by 6.2% from baseline versus placebo, demonstrating superiority over placebo ($p = 0.0067$). For the 2-gram group, LDL-C decreased by 3.6% from baseline versus placebo ($p = 0.0867$), which is not a statistically significant decrease.

Other secondary efficacy endpoints included the median placebo-adjusted percent change in non-high-density lipoprotein cholesterol (non-HDL-C), apolipoprotein B (apo B), and lipoprotein-associated phospholipase A2 (Lp-PLA2). The 4-gram dose was associated with statistically significant reductions in non-HDL-C (13.6%, $p < 0.0001$), apo B (9.3%, $p < 0.0001$), Lp-PLA2 (19%, $p < 0.0001$) and high-sensitivity C-reactive protein (hsCRP) (22%, $p < 0.001$), at week 12 compared to placebo. One published analysis showed that the Vascepa 4-gram daily dose in the ANCHOR study also significantly decreased levels of the inflammatory marker oxidized low-density lipoprotein relative to placebo by 13% ($p < 0.0001$). In a separate, post-hoc analysis of study data, Vascepa 4 g/day statistically significantly reduced ApoC-III levels by 25.1% in MARINE ($p < 0.0001$) and by 19.2% in ANCHOR ($p < 0.0001$) versus placebo.

Vascepa was well tolerated in the ANCHOR trial with a safety profile comparable to placebo and there were no treatment-related serious adverse events observed. No significant changes in fasting blood glucose, hemoglobin A1C, vital signs, electrocardiograms, or liver or kidney function were observed with either Vascepa dose. The safety results from the ANCHOR trial are included in the current FDA-approved label for Vascepa.

In April 2015, we received a Complete Response Letter, or CRL, from the FDA in response to our supplemental new drug application, or sNDA, that sought approval of Vascepa for use in patients with mixed dyslipidemia, based on the successful ANCHOR study. The CRL followed an October 2013 rescission by the FDA of a SPA agreement and three failed attempts by us to appeal that rescission at FDA. The FDA has acknowledged the success of the ANCHOR study, which met all primary and secondary endpoints.

However, FDA determined that there were insufficient data to conclude that drug-induced changes in serum triglycerides could be recognized by the FDA as a valid surrogate for reducing cardiovascular risk in the ANCHOR population for the purpose of regulatory approval of a drug targeted at a triglyceride-lowering indication in this population. The FDA has acknowledged that the standard of proof required by the FDA for approval of a new drug indication is higher than that generally used to inform patient treatment guidelines and that used by physicians in clinical practice. The FDA did not determine that the drug-induced effects of Vascepa, which go beyond triglyceride-lowering, would not actually reduce cardiovascular risk in this population and the FDA has encouraged us to complete the REDUCE-IT outcomes study. Based on our communications with the FDA, it has been our expectation that submission of final positive results from the REDUCE-IT outcomes study is required for the FDA to consider label expansion for Vascepa.

In May 2015, we and a group of independent physicians filed a lawsuit in federal court to permit us to promote to healthcare professionals the use of Vascepa in patients with mixed dyslipidemia so long as the promotion is truthful and non-misleading. This use reflects recognized medical practice but is not covered by current FDA-approved labeling for the drug. Historically, FDA has considered promotion of drug uses not covered by FDA-approved labeling to be illegal off-label promotion, even if such promotion is truthful and non-misleading. In August 2015, we were granted preliminary relief in the form of a declaratory judgment in this lawsuit. The court declaration permits us to promote to healthcare professionals the FDA-reviewed and agreed effects of Vascepa demonstrated in the ANCHOR clinical trial and presentation of the current state of scientific research related to the potential of Vascepa to reduce the risk of cardiovascular disease including through use of peer-reviewed scientific publications of available data. In August 2015, we began to communicate promotional information beyond the MARINE indication to healthcare professionals in the United States as permitted by this court declaration and in March 2016, the parties obtained court approval of negotiated settlement terms under which the FDA and the U.S. government agreed to be bound by the court's conclusions from the August 2015 declaration that we may engage in truthful and non-misleading speech promoting the off-label use of Vascepa and that certain statements and disclosures that we proposed to make to healthcare professionals were truthful and non-misleading. While we believe we are now permitted under applicable law to more broadly promote Vascepa, the FDA-approved labeling for Vascepa did not change as a result of this litigation and settlement, and neither government nor other third-party coverage or reimbursement to pay for the off-label use of Vascepa promoted under the court declaration was required.

The REDUCE-IT Study (the completed cardiovascular outcomes study)

The REDUCE-IT study was designed to evaluate the efficacy of Vascepa in reducing major cardiovascular events in an at-risk patient population also receiving statin therapy. REDUCE-IT was a multinational, prospective, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the effectiveness of Vascepa, as an add-on to statin therapy, in reducing first major cardiovascular events in an at-risk patient population compared to statin therapy alone. The control arm of the study was comprised of patients on optimized statin therapy plus placebo. The active arm of the study was comprised of patients on optimized statin therapy plus Vascepa. All subjects enrolled in the study had elevated triglyceride levels and either established coronary heart disease or risk factors for coronary heart disease.

In August 2011, we reached agreement with the FDA on a SPA for the design of the REDUCE-IT (Reduction of Cardiovascular Events with EPA—Intervention Trial) cardiovascular outcomes study. A 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. The FDA agreed that, based on the information we submitted to the agency, the design and planned analysis of the REDUCE-IT study adequately addressed the objectives necessary to support a regulatory submission. A SPA is generally binding upon the FDA unless a substantial scientific issue essential to determining safety or efficacy of the drug is identified after the testing begins.

It is believed that the effects of EPA are not due to a single mode of action, such as triglyceride lowering, but rather to multiple mechanisms working together. Studies in the scientific literature explore potentially beneficial effects of EPA on multiple atherosclerosis processes, including endothelial function, oxidative stress, foam cell formation, inflammation/cytokines, plaque formation/progression, platelet aggregation, thrombus formation, and plaque rupture. With respect to triglyceride levels, our scientific rationale for the REDUCE-IT study was supported by (i) epidemiological data that suggests elevated triglyceride levels correlate with increased cardiovascular disease risk, (ii) genetic data that suggests triglyceride and/or triglyceride-rich lipoproteins (as well as low-density lipoprotein cholesterol (LDL cholesterol), known as bad cholesterol) are independently in the causal pathway for cardiovascular disease and (iii) clinical data that suggest substantial triglyceride reduction in patients with elevated baseline triglyceride levels correlates with reduced cardiovascular risk. The REDUCE-IT study was designed to determine the clinical benefit, if any, of stable EPA therapy in statin-treated patients with elevated triglyceride levels.

In September 2011, we engaged a clinical research organization, or CRO, and began initial trial and clinical site preparation for REDUCE-IT. In December 2011, we announced that the first patient was dosed in the study. In 2016, we completed patient enrollment and randomization of 8,179 individual patients into the REDUCE-IT study. Amarin personnel remained blinded to the efficacy and safety data from the REDUCE-IT study until after the study was completed and the database was locked in 2018.

On November 10, 2018, we announced primary results from our REDUCE-IT study as late-breaking clinical results at the 2018 Scientific Sessions of the American Heart Association and the results were concurrently published in The New England Journal of Medicine. REDUCE-IT met its primary endpoint demonstrating a 25% relative risk reduction, or RRR, to a high degree of statistical significance ($p < 0.001$), in first occurrence of major adverse CV events, or MACE, in the intent-to-treat patient population with use of Vascepa 4 grams/day as compared to placebo. Patients qualified to enroll in REDUCE-IT had LDL-C between 41-100 mg/dL (median baseline LDL-C 75 mg/dL) controlled by statin therapy and various cardiovascular risk factors including persistent elevated triglycerides, or TG, between 135-499 mg/dL (median baseline 216 mg/dL) and either established cardiovascular disease (secondary prevention cohort) or age 50 or more with diabetes mellitus and at least one other CV risk factor (primary prevention cohort). Approximately 59% of the patients had diabetes at baseline, approximately 71% of the patients had established cardiovascular disease at time of enrollment and approximately 29% were primary prevention subjects at high risk for cardiovascular disease. REDUCE-IT also showed a 26% RRR in its key secondary composite endpoint of cardiovascular death, heart attacks and stroke ($p < 0.001$). We commenced the REDUCE-IT trial in 2011 and have expended more than \$300 million to fund its completion.

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

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

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

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

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

Positive REDUCE-IT results were consistent across various patient subgroups, including female/male, diabetic/non-diabetic and secondary/primary prevention.

Overall adverse event rates in REDUCE-IT were similar across treatment groups and Vascepa was well tolerated with a safety profile generally consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labeling of such products. The safety results from REDUCE-IT are reviewed in The New England Journal of Medicine publication of REDUCE-IT results.

In the REDUCE-IT trial, cardiovascular benefits appeared not to be influenced significantly by TG levels at baseline (above or below 150 mg/dL baseline range) or as achieved at one year, potentially suggesting mechanisms at work with use of Vascepa that are independent of baseline TG levels or therapy-driven reduction in TG levels. Determining the mechanisms responsible for the benefit shown in REDUCE-IT was not the focus of REDUCE-IT. As summarized from the primary results of REDUCE-IT in The New England Journal of Medicine, potential Vascepa mechanisms of action at work in REDUCE-IT may include TG reduction, anti-thrombotic effects, antiplatelet or anticoagulant effects, membrane-stabilizing effects, effects on stabilization and/or regression of coronary plaque and inflammation reduction, each as supported by earlier stage mechanistic studies.

In addition, in the REDUCE-IT trial, the median change in LDL cholesterol levels from baseline was higher in the placebo group versus the Vascepa group (difference of 5.0 mg/dL; $p < 0.001$). However, a post hoc analysis of REDUCE-IT data, as published in The New England Journal of Medicine, showed no material difference in each of the primary and key secondary cardiovascular risk composite endpoint event rates for placebo patients that experienced an increase in LDL-C at one year versus those with no change or a decrease, and also suggested a similar relative risk reduction regardless of whether there was an increase in LDL cholesterol level among the patients in the placebo group. Moreover, as the authors of the paper published in The New England Journal of Medicine noted, the relatively small differences in LDL-C levels between the groups would not be likely to explain the 25% lower

MACE risk observed with Vascepa and the Japan open-label EPA Lipid Intervention Study, or JELIS, an over 18,000 patient cardiovascular outcomes study in Japan of a highly-pure EPA product similar to Vascepa, previously demonstrated a 19% risk reduction without a mineral oil placebo.

Based on the positive REDUCE-IT results, we have begun promoting REDUCE-IT results to healthcare professionals in the United States based on what we believe is our continuing obligation under our First Amendment settlement to ensure that our promotion of Vascepa remains truthful and non-misleading.

We anticipate continuing to publish additional details of the REDUCE-IT study to address scientific interest beyond the primary results of this study derived from the over 35,000 patient years of study accumulated.

Regulatory Pathway for REDUCE-IT Data

We intend to submit an sNDA to the FDA before the end of March 2019 seeking approval to expand the label for Vascepa based on the effects of Vascepa demonstrated in the REDUCE-IT study. The FDA's determination of standard or priority review will be made when the sNDA is submitted. At this time, we are planning for a standard review with a PDUFA date which is approximately 10-months after the date of the sNDA submission.

Observed Efficacy of Ethyl-EPA

In Japan, ethyl-EPA is marketed under the product name of Epadel by Mochida Pharmaceutical Co. and is indicated for hyperlipidemia and peripheral vascular disease. In an outcomes study called the Japan EPA Lipid Intervention Study, or JELIS study, which consisted of more than 18,000 patients followed over multiple years, Epadel, when used in conjunction with statins, was shown to reduce cardiovascular events by 19% compared to the use of statins alone. In this study, cardiovascular events decreased by approximately 53% compared to statins alone in the subset of primary prevention patients with triglyceride levels of ≥ 150 mg/dL (median of 272 mg/dL at entry) and HDL-C < 40 mg/dL. Epadel has been approved and available by prescription in Japan for over a decade. In 2013, the Japan Ministry of Health approved Epadel for over-the-counter sales. JELIS provided supportive but not conclusive data that EPA drug therapy may reduce major coronary events. JELIS results cannot be generalized to populations outside of Japan due to limitations in the study's design. Due to the limitation of JELIS, further study was needed through the REDUCE-IT study to determine the clinical benefit, if any, of EPA therapy in statin-treated patients with elevated triglyceride levels in a patient population beyond that studied in JELIS.

Observed Clinical Safety of Vascepa

In REDUCE-IT, Vascepa was well tolerated with a safety profile generally consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labeling of such products. Excluding the MACE results described above, overall adverse event rates in REDUCE-IT were similar across the statin plus Vascepa and the statin plus placebo treatment groups. There were no significant differences between treatments in the overall rate of treatment emergent adverse events or serious adverse events leading to withdrawal of study drug. The one serious adverse event occurring at a frequency of $> 2\%$ was pneumonia which occurred at a numerically higher rate in the statin plus placebo treatment group (2.9%) than in the statin plus Vascepa treatment group (2.6%). Adverse events occurring in 5% or greater of patients and more frequently with Vascepa than placebo were peripheral edema (6.5% Vascepa patients versus 5.0% placebo patients), constipation (5.4% Vascepa patients versus 3.6% placebo patients), and atrial fibrillation (5.3% Vascepa patients versus 3.9% placebo patients). There were numerically more serious adverse events related to bleeding in the statin plus Vascepa treatment group although overall rates were low with no fatal bleeding observed in either group and no significant difference in adjudicated hemorrhagic stroke or serious central nervous system or gastrointestinal bleeding events between treatments.

In the MARINE and ANCHOR trials, patients dosed with Vascepa demonstrated a safety profile similar to placebo. There were no treatment-related serious adverse events in the MARINE study or in the ANCHOR study. In the MARINE and ANCHOR trials, the most commonly reported adverse reaction (incidence >2% and greater than placebo) in Vascepa treated patients was arthralgia (joint pain) (2.3% for Vascepa vs. 1.0% for placebo). There was no reported adverse reaction > 3% and greater than placebo.

Prior to commencing the MARINE, ANCHOR and REDUCE-IT trials, we conducted a pre-clinical program for Vascepa, including toxicology and pharmacology studies. In addition, we previously investigated Vascepa in central nervous system disorders in several double-blind, placebo-controlled studies, including Phase 3 trials in Huntington's disease. Over 1,000 patients have been dosed with Vascepa in these studies, with over 100 receiving continuous treatment for a year or more. In all studies performed to date, Vascepa has shown a favorable safety and tolerability profile.

In addition to the MARINE and ANCHOR trials, we completed a 28-day pharmacokinetic study in healthy volunteers, a 26-week study to evaluate the toxicity of Vascepa in transgenic mice and multiple pharmacokinetic drug-drug interaction studies in

healthy subjects in which we evaluated the effect of Vascepa on certain common prescription drugs. All findings from these studies were consistent with our expectations and confirmed the overall safety profile of Vascepa.

Since Vascepa was made commercially available in 2013, more than five million estimated normalized total prescriptions of Vascepa have been reported by Symphony Health.

New Lipid Compounds and other Preclinical Programs

We are also considering development of other next generation compounds based on our internal lipid science expertise, including potential combination and derivative therapies.

In August 2013, we completed dosing of AMR102, a fixed dose combination of Vascepa and a leading statin product. The study is a randomized, open-label, single-dose, 4-way cross-over study to continue testing of the relative bioavailability of AMR102 capsules, Vascepa capsules with the selected statin taken concomitantly, Vascepa taken alone and the selected statin taken alone. The results of this study support the feasibility of AMR102. We have suspended additional development of AMR102 pending FDA approval of label expansion of Vascepa, anticipated to occur no sooner than after FDA review of the results from the REDUCE-IT study.

We believe that Vascepa and other lipid-based compositions may have an impact on a number of biological factors in the body such as anti-inflammatory mechanisms, cell membrane composition and plasticity, triglyceride levels and regulation of glucose metabolism. Currently all other development activities are at formulation or pre-clinical stages.

Manufacturing and Supply for Vascepa

We manage the manufacturing and supply of Vascepa and have done so since we began clinical development of Vascepa prior to the drug's marketing approval by the FDA in 2012. We rely on contract manufacturers in each step of our commercial and clinical product supply chain. These steps include active pharmaceutical ingredient, or API, manufacturing, encapsulation of the API, product packaging and supply-related logistics. Our approach to product supply procurement is designed to mitigate risk of supply interruption and maintain an environment of cost competition through diversification of contract manufacturers at each stage of the supply chain and lack of reliance on any single supplier.

The FDA has approved several international large-scale API manufacturers, global encapsulation leaders and two U.S.-based packagers for use in the manufacturing of Vascepa. All of our manufacturing facilities were approved by the FDA following successful preapproval inspections and they remain active manufacturers of Vascepa under FDA authority.

The API material that constitutes ethyl-EPA is a chemical modification of a naturally occurring substance that is derived from specific fish sourced from qualified producers. The fishing from which the raw material for Vascepa is derived is regulated by local government agencies under policies designed to ensure sustainability of the marine life supply. A limited number of other manufacturers have the ability, scale, know-how, sufficient supply chain capability and suitable, industrial-scale facilities to produce ethyl-EPA to the required level of purity. Among the conditions for FDA approval of a pharmaceutical product is the requirement that the manufacturer's quality control and manufacturing procedures are validated and conform to pharmaceutical current Good Manufacturing Practice, or cGMP, which, under applicable regulations, must be followed at all times. The FDA typically inspects manufacturing facilities before regulatory approval of a product candidate, such as Vascepa, and on a periodic basis after the initial approval. Consistent with cGMP regulations, pharmaceutical manufacturers must expend resources and time to ensure

compliance with product specifications as well as production, record keeping, quality control, reporting, and other regulatory requirements.

Some of our agreements with our API suppliers are exclusive and include minimum purchase commitments. During 2018, we fully met the aggregate minimum purchase requirements in our supply agreements. Under the supply agreements, we can purchase more than the minimum requirements. Certain of these agreements contemplate phased capacity expansion aimed at creating sufficient volumes to meet anticipated demand for Vascepa. Certain of these agreements contain provisions for reduced payments (fractional API cost) for unmet annual volume requirements.

Our Commercialization Plans

We currently market Vascepa in the United States through our direct sales force which grew from approximately 170 sales professionals, including sales representatives and their managers, in September 2018 prior to REDUCE-IT results to approximately 440 sales professionals, including approximately 400 sales representatives, to begin 2019. We currently target clinicians who are top prescribers of lipid-regulating therapies, including statins. During the period from January 2013, when Vascepa was commercially launched in the United States, until October 2013, when the FDA notified us that it rescinded the ANCHOR study SPA agreement, our direct sales force consisted of approximately 275 sales representatives. From early 2014 until September 2018, the size of our direct sales force has included approximately 130 to 150 sales representatives with focus on select sales territories that have the greatest

potential for Vascepa sales growth. After topline REDUCE-IT results were announced in September 2018, we began to hire and train additional sales representatives and started 2019 with approximately 400 sales representatives.

From May 2014 through December 2018, in addition to Vascepa promotion by our sales representatives, Kowa Pharmaceuticals America, Inc. co-promoted Vascepa in the United States. This co-promotion reached its mutually agreed upon termination date in December 2018.

We also employ various medical affairs and marketing personnel to support our commercialization of Vascepa. We expanded certain medical education and market awareness initiatives, including, pilot testing of new promotional initiatives following the reporting of positive REDUCE-IT results in 2018 and we intend to further expand such initiatives following label expansion of Vascepa, subject to FDA approval of such expanded label, as discussed below. Our field sales efforts are further complemented by investments in digital and non-personal channels as well as peer-to-peer (e.g., promotional medical education programs & product theaters) initiatives to further increase Vascepa brand awareness and clarify Vascepa's unique clinical profile.

Since commercial launch of Vascepa in January 2013, we have promoted Vascepa based on the MARINE clinical trial data as reflected in the FDA-approved label for Vascepa. In August 2015, we and our co-promotion partner began communicating promotional information beyond MARINE clinical trial data to targeted healthcare professionals. Such qualified communications are being made pursuant to the August 7, 2015 federal district court declaration and related March 2016 settlement allowing truthful and non-misleading promotion of the FDA-reviewed and agreed effects of Vascepa demonstrated in the ANCHOR clinical trial. This promotion also includes information related to the current state of scientific research about the potential of Vascepa to reduce the risk of cardiovascular disease, including REDUCE-IT data and previously other peer-reviewed scientific publications of available data.

After results of REDUCE-IT were available in September 2018 and demonstrated that Vascepa is effective in lowering the rate of major adverse cardiovascular events in statin-treated patients with CV risk factors, we expanded the size of our U.S. direct sales force and continue to expand promotion of Vascepa based on the results of the REDUCE-IT trial. After publication of the primary results of the REDUCE-IT study in *The New England Journal of Medicine* and scientific presentation of REDUCE-IT results at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018, we updated and expanded our communication of REDUCE-IT results to include the publication and the peer-reviewed information presented in an effort to further ensure that our communications remain truthful and non-misleading.

The dataset from Vascepa is large, representing greater than 35,000 patient years of study. Additionally, the list of prespecified endpoints which we intend to evaluate in support of the sNDA is extensive. We intend to submit an sNDA to the FDA in the United States before the end of March 2019 seeking approval to expand the label for Vascepa based on the effects of Vascepa demonstrated in the REDUCE-IT study. Assuming a standard 10-month review by the FDA, we do not expect an expanded label for Vascepa to be available in 2019 or to impact 2019 Vascepa revenue levels. After the sNDA is submitted, Amarin will seek clarification as to whether priority review by the FDA is possible for this important submission.

Throughout 2019, we expect to continue an efficient expansion of our commercial activities and capabilities directed primarily toward targeted providers and payor decision-makers. We plan to continue to bring the results of REDUCE-IT to healthcare providers and payors, in a manner we believe is both truthful and non-misleading and consistent with our March 2016 settlement. Thus, we are directly connecting Vascepa with the REDUCE-IT data for these target audiences, in advance of having a new label. Further, anticipating the potential receipt of a new, cardiovascular risk reduction indication in the United States, we are preparing a robust, direct to consumer campaign to be launched in earnest after receiving a new label. Concurrently, we also will reassess whether approximately 440 sales professionals, including approximately 400 sales representatives, in conjunction with planned medical education,

digital and non-personal outreach levels are adequate and invest appropriately to support the multi-billion-dollar potential of this important new cardiovascular therapy.

Outside of the United States, we have expanded our commercialization activities through partnering arrangements in certain territories. In February 2015, we entered into a Development, Commercialization and Supply Agreement, or the DCS Agreement, with Eddingpharm (Asia) Macao Commercial Offshore Limited, or Eddingpharm, related to the development and commercialization of Vascepa in Mainland China, Hong Kong, Macau and Taiwan, or the China Territory. Under the DCS Agreement, Eddingpharm will be solely responsible for development and commercialization activities in the China Territory and associated expenses. Additionally, Eddingpharm is required to conduct clinical trials in the China Territory to secure regulatory approval in certain territories. For example, in December 2017, Eddingpharm commenced a pivotal clinical trial aimed to support the regulatory approval of the first indication of Vascepa in a patient population with severe hypertriglyceridemia in Mainland China. Additional clinical development efforts may be necessary in this market. Significant commercialization of Vascepa in the China Territory is several years away, if at all. If Eddingpharm is not able to effectively develop and commercialize Vascepa in the China Territory, we may not be able to generate revenue from the DCS Agreement resulting from the sale of Vascepa in the China Territory.

In March 2016, we entered into an agreement with Biologix FZCo, or Biologix, to register and commercialize Vascepa in several Middle Eastern and North African countries. Under the terms of the distribution agreement, we granted to Biologix a non-

exclusive license to use our trademarks in connection with the importation, distribution, promotion, marketing and sale of Vascepa in the Middle East and North Africa territory. Commercialization across the Middle East and North Africa is several years away, if at all, in the most commercially significant territories and subject to similar risks as in the China Territory.

In September 2017, we entered into an agreement with HLS Therapeutics Inc., or HLS, to register, commercialize and distribute Vascepa in Canada. Under the agreement, HLS will be responsible for regulatory and commercialization activities and associated costs. We will be responsible for providing assistance towards local filings, supplying finished product under negotiated supply terms, maintaining intellectual property, and continuing the development and funding of REDUCE-IT. Significant commercialization of Vascepa in Canada is years away, if at all. If HLS Therapeutics is not able to effectively register and commercialize Vascepa in Canada, we may not be able to generate revenue from the agreement as a result of the sale of Vascepa in Canada.

We continue to assess other partnership opportunities for licensing Vascepa to partners outside of the United States.

Competition

The biotechnology and pharmaceutical industries are highly competitive. There are many pharmaceutical companies, biotechnology companies, public and private universities and research organizations actively engaged in the research and development of products that may be similar to our products. It is probable that the number of companies seeking to develop products and therapies similar to our products will increase. Many of these and other existing or potential competitors have substantially greater financial, technical and human resources than we do and may be better equipped to develop, manufacture and market products. These companies may develop and introduce products and processes competitive with or superior to ours. In addition, other technologies or products may be developed that have an entirely different approach or means of accomplishing the intended purposes of our products, which might render our technology and products noncompetitive or obsolete.

Our competitors both in the United States and abroad include large, well-established pharmaceutical and generic companies, specialty and generic pharmaceutical sales and marketing companies, and specialized cardiovascular treatment companies. GlaxoSmithKline plc currently sells Lovaza[®], a prescription-only omega-3 fatty acid indicated for patients with severe hypertriglyceridemia, which was approved by FDA in 2004 and has been on the market in the United States since 2005. Multiple generic versions of Lovaza are available in the United States. Other large companies with competitive products include AbbVie, Inc., which currently sells Tricor[®] and Trilipix[®] for the treatment of severe hypertriglyceridemia and Niaspan[®], which is primarily used to raise high-density lipoprotein cholesterol, or HDL-C, but is also used to lower triglycerides. Multiple generic versions of Tricor, Trilipix and Niaspan are also available in the United States. We compete with these drugs, and in particular, multiple low-cost generic versions of these drugs, in our FDA-approved indicated use and in off-label uses, such as to beneficially affect lipid levels in patients with persistent high triglyceride levels after statin therapy with the aim of potentially lowering cardiovascular risk beyond statin therapy.

In addition, in May 2014, Epanova[®] (omega-3-carboxylic acids) capsules, a free fatty acid form of omega-3 (comprised of 55% EPA and 20% DHA), was approved by the FDA for patients with severe hypertriglyceridemia. Epanova was developed by Omthera Pharmaceuticals, Inc., and is now owned by AstraZeneca Pharmaceuticals LP (AstraZeneca). Also, in April 2014, Omtryg, another omega-3-acid fatty acid composition developed by Trygg Pharma AS, received FDA approval for severe hypertriglyceridemia. Neither Epanova nor Omtryg have been commercially launched, but could launch at any time. Each of these competitors, other than Trygg, has greater resources than we do, including financial, product development, marketing, personnel and other resources. Neither Epanova nor Omtryg have been commercially launched.

AstraZeneca is currently conducting a long-term outcomes study to assess Statin Residual Risk Reduction With Epanova in High Cardiovascular Risk Patients With Hypertriglyceridemia (STRENGTH). The study is a randomized, double-blind, placebo-controlled (corn oil), parallel group design that is believed to have enrolled approximately 13,000 patients with hypertriglyceridemia and low HDL and high risk for cardiovascular disease randomized 1:1 to either corn oil plus statin or Epanova plus statin, once daily, for approximately 3-5 years as determined when the number of major adverse cardiovascular event outcomes is reached. The STRENGTH study is estimated to be completed in 2020, but it could be stopped earlier if, for example, it generates an overwhelming efficacy result. In addition, Kowa Research Institute (a subsidiary of the Japanese company Kowa Co., Ltd) announced in March 2017 that it is initiating a phase III cardiovascular outcomes trial titled PROMINENT examining the effect of pemafibrate (experimental name K-877) in reducing cardiovascular events in Type II diabetic patients with hypertriglyceridemia. Kowa Research Institute has publicly estimated study completion in May 2022, and if successful, U.S. regulatory approval is estimated in mid-2023.

During 2018, two outcomes studies were completed of omega-3 mixtures which both failed to achieve their primary endpoints of cardiovascular risk reduction and two meta-analyses were published showing that omega-3 mixtures are not effective in lowering cardiovascular risk. Results of these failed outcomes studies and analysis, while not done with Vascepa, may negatively affect sales of Vascepa. For example, results of VITamin D and Omega-3 Trial (VITAL), as announced immediately before the presentation of REDUCE-IT results at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018, failed to achieve its primary endpoint of lowering cardiovascular events. VITAL was an NIH funded randomized double-blind, placebo-controlled, 2x2 factorial trial of 2000 IU per day of vitamin D3 and 1 gram per day of omega-3 fatty acid supplementation (Lovaza)

for the primary prevention of cancer and cardiovascular disease in a nationwide USA cohort of 25,874 adults not selected for elevated cardiovascular or cancer risk.

Likewise, in 2018, results from A Study of Cardiovascular Events in Diabetes (ASCEND) trial were released and showed negligible results for omega-3 fatty acids 1 gram daily. ASCEND was a British Heart Foundation funded 2x2 factorial design, randomized study to assess whether aspirin 100 mg daily versus placebo and separately, omega-3 fatty acids 1 gram daily versus placebo, reduce the risk of cardiovascular events in a nationwide UK cohort of over 15,000 individuals with diabetes who do not have atherosclerotic cardiovascular disease. In addition, VITAL showed that supplementation with either omega-3 fatty acid at a dose of 1 gram per day or vitamin D3 at a dose of 2000 IU per day was not effective for primary prevention of CV or cancer events among healthy middle-aged men and women across 5 years of follow up.

In meta-analysis, presented in 2018 by the Cochran Foundation and separately as published in JAMA, additional omega-3 studies were evaluated. Similar to the VITAL and ASCEND studies, most of the studies in these omega-3 meta-analyses were of omega-3 mixtures, including DHA, and most were studies of relatively low doses of omega-3 as is associated with dietary supplementation and/or they studied relatively low risk patient populations. The exception was the JELIS study, conducted in Japan, of highly pure EPA which demonstrated a positive outcome benefit. The negative results from such omega-3 mixture studies could create misleading impressions about the use of omega-3s generally, including Vascepa, despite REDUCE-IT positive results and the highly-pure and stable EPA active ingredient in Vascepa and its higher dose regimen.

We are also aware of other pharmaceutical companies that are developing products that, if successfully developed, approved and marketed, would compete with Vascepa. Acasti Pharma, or Acasti, a subsidiary of Neptune Technologies & Bioresources Inc., announced in December 2015 that it intends to pursue a regulatory pathway under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, or FDCA, for its omega-3 prescription drug candidate, CaPre[®] (omega-3 phospholipid), derived from krill oil, for the treatment of hypertriglyceridemia. In September 2016, Acasti announced positive results from its pivotal bioavailability bridging study comparing CaPre to Lovaza, establishing a scientific bridge between the two that is expected to support the feasibility of a 505(b)(2) regulatory pathway. Acasti initiated a Phase 3 clinical program (TRILOGY) to assess the safety and efficacy of CaPre in patients with very high (≥ 500 mg/dL) triglycerides in the first quarter of 2018. Acasti completed enrollment in Q4 2018 and study completion is expected by the end of 2019. We believe Micelle BioPharma Inc., or Micelle, is also developing potential treatments for hypertriglyceridemia based on omega-3 fatty acids. To our knowledge, Micelle, after acquiring SC401 from Sancilio & Company, or Sancilio, is pursuing a regulatory pathway under section 505(b)(2) of the FDCA for its product and submitted an Investigational New Drug Application, or IND, in July 2015. Micelle (Sancilio) completed two pharmacokinetic studies and Phase 2 bioavailability studies (FASTR I&II), with one comparing SC401 to Lovaza. We expect the company or a potential partner to initiate a pivotal clinical Phase 3 study as the next step in development.

Matinas BioPharma, Inc. is developing an omega-3-based therapeutic (MAT9001) for the treatment of severe hypertriglyceridemia and mixed dyslipidemia. In the fourth quarter of 2014, Matinas BioPharma, Inc. filed an IND with the FDA to conduct a human study in the treatment of severe hypertriglyceridemia and, in June 2015, the company announced topline results for its head-to-head comparative short duration pharmacokinetic and pharmacodynamic study of MAT9001 versus Vascepa in patients under conditions inconsistent with the FDA-approved label for Vascepa and presented results based on biomarker modification without outcomes data. In September 2017, Matinas announced that it will be seeking a partner company to develop and commercialize MAT9001. Akcea Therapeutics/Ionis Pharmaceuticals (formerly Isis Pharmaceuticals), or Akcea/Ionis, in August 2018 announced the receipt of a complete response letter from the FDA for WAYLIVRA[™] (volanesorsen), a drug candidate administered through weekly subcutaneous injections, for the treatment of familial chylomicronemia syndrome (FCS). Akcea will continue to work with the FDA on the path forward for Waylivra for the treatment of

FCS. Waylivra continues to be developed for the treatment of familial partial lipodystrophy (FPL).

A Phase 3 trial is currently ongoing studying Waylivra (volanesorsen) in patients with FPL (BROADEN trial). Akcea/Ionis expects to file an NDA for FPL in 2019. In January 2017, Akcea/Ionis announced a strategic collaboration and option agreement with Novartis whereby Novartis will help develop (including funding cardiovascular outcomes studies) and commercialize products emerging from this collaboration, including Waylivra (volanesorsen). In June 2018, Gemphire Therapeutics announced positive topline results from a Phase 2b trial (INDIGO-1) of its drug candidate, gemcabene, in patients with severe hypertriglyceridemia. Gemcabene is an oral, once-daily pill for a number of hypercholesterolemic populations and severe hypertriglyceridemia. Gemphire announced plans to initiate a Phase III study for homozygous familial hypercholesterolemia (HoFH), heterozygous familial hypercholesterolemia (HeFH) and non-familial hypercholesterolemia in ASCVD patients in the second half of 2018. In August 2018, the FDA requested that Gemphire conduct an additional long-term toxicity study before commencing any further clinical testing, thereby effectively placing gemcabene on clinical hold. Zydus Cadila has a Phase 2 development program for its lead molecule, Saroglitazar, in various indications, including severe hypertriglyceridemia in the United States. In August 2018, the Company announced that it had suspended the Phase 2 trial in the severe hypertriglyceridemia indication due to study enrollment issues, while it continues development activities in other indications. The product is approved in India under the name Lipaglyn® for the treatment of hypertriglyceridemia and diabetic dyslipidemia. We are also aware that bezafibrate has been licensed by Intercept Pharmaceuticals to be further developed and potentially launched in the United States market.

Based on prior communications from the FDA, including communications in connection with its review of the ANCHOR indication for Vascepa, it is our understanding that the FDA is not prepared to approve any therapy for treatment of cardiovascular risk based on biomarker modification without outcomes study data, with the potential exception of therapies which lower LDL-cholesterol. In particular, it is our understanding that the FDA is not prepared to approve any therapy based on data demonstrating lowering of triglyceride levels. In our view, this position from the FDA is unlikely to change based on the REDUCE-IT study particularly in light of the independence of the positive benefit demonstrated in the REDUCE-IT study from triglyceride levels and benefit from the REDUCE-IT study supporting that the positive effects of Vascepa are unique to Vascepa and extend beyond triglyceride reduction. If the FDA were to change this position, it could potentially have a negative impact on Amarin by making it easier for other products to achieve a cardiovascular risk reduction indication without the need in advance to conduct a long and expensive cardiovascular outcomes study

Vascepa also faces competition from dietary supplement companies marketing omega-3 products as nutritional supplements. Such products are classified as food, not as prescription drugs or as over-the-counter drugs, by the FDA. Many of the promoters of such products have greater resources than Amarin and they are not restricted to the same standards as are prescription drugs with respect to promotional claims or manufacturing quality, consistency and subsequent product stability. Though we have taken legal action against supplement manufacturers attempting to use the REDUCE-IT results to promote their products, we cannot be sure physicians and pharmacists will view the FDA-approved prescription-only status, EPA-only purity of Vascepa and stringent regulatory oversight as significant advantages versus omega-3 dietary supplements regardless of clinical study results and other scientific data.

In addition, several generic drug companies have sought to challenge the validity and enforceability of our patents and have submitted to FDA applications for approval of generic versions of Vascepa.

Regulatory Matters

Government Regulation and Regulatory Matters

Any product development activities related to Vascepa or products that we may develop or acquire in the future will be subject to extensive regulation by various government authorities, including the FDA and comparable regulatory authorities in other countries, which regulate the design, research, clinical and non-clinical development, testing, manufacturing, storage, distribution, import, export, labeling, advertising and marketing of pharmaceutical products and devices. Generally, before a new drug can be sold, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review and approved by the regulatory authority. The data is generated in two distinct development stages: pre-clinical and clinical. Drugs must be approved by the FDA through the NDA process before they are first marketed in the United States. For new chemical entities, the pre-clinical development stage generally involves synthesizing the active component, developing the formulation, determining the manufacturing process and controls, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies which support subsequent clinical testing.

The clinical stage of development can generally be divided into Phase 1, Phase 2 and Phase 3 clinical trials. In Phase 1, generally, a small number of healthy volunteers are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these studies is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug. Phase 2 trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected. Phase 3 trials generally involve large numbers of patients at multiple sites, in multiple countries and are designed to provide the pivotal data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use, and may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

United States Drug Development

In the United States, the process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Prior to the start of human clinical studies for a new drug in the United States, preclinical laboratory and animal tests are often performed under the FDA's Good Laboratory Practices regulations, or GLP, and an investigational new drug application, or IND, is filed with the FDA. Similar filings are required in other countries; however, data requirements and other information needed for a complete submission may differ in other countries. The amount of data that must be supplied in the IND depends on the phase of the

study. Phase 1 studies typically require less data than larger Phase 3 studies. A clinical plan must be submitted to the FDA prior to commencement of a clinical trial. If the FDA has concerns about the clinical plan or the safety of the proposed studies, it may suspend or terminate the study at any time. Studies must be conducted in accordance with Good Clinical Practice, or GCP, and regular reporting of study progress and any adverse experiences is required. Studies are also subject to review by independent institutional review boards, or IRBs, responsible for overseeing studies at particular sites and protecting human research study subjects. An independent IRB may also suspend or terminate a study once initiated.

NDA and FDA Review Process

Following trial completion, trial data is analyzed to determine safety and efficacy. Data is then filed with the FDA in an NDA along with proposed labeling for the product and information about the manufacturing and testing processes and facilities that will be used to ensure product quality. The NDA must contain proof of safety, purity, potency and efficacy, which entails extensive pre-clinical and clinical testing. FDA approval of an NDA must be obtained before first marketing of a drug in the United States.

The FDA will likely re-analyze the clinical trial data, which could result in iterative discussions between the FDA and us during the review process. The review and evaluation of applications by the FDA is extensive and time consuming and may take longer than originally planned to complete. The FDA may conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with current Good Manufacturing Practice, or cGMP, requirements and may also audit data from clinical and pre-clinical trials.

There is no assurance that the FDA will ultimately approve a drug product for marketing in the United States. Even if future indications for Vascepa are approved, the FDA's review will be lengthy, and we may encounter significant difficulties or costs during the review process. After approving any drug product, the FDA may require post-marketing testing and surveillance to monitor the effects of approved products or it may place conditions on approvals including potential requirements or risk management plans that could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

Off-label Promotion in the United States

The Federal Food, Drug, and Cosmetic Act, or FDCA, has been interpreted by the FDA and the U.S. government to make it illegal for pharmaceutical companies to promote their FDA-approved products for uses that have not been approved by the FDA. Companies that market drugs for off-label uses or indications have been subject to related costly litigation, criminal penalties and civil liability under the FDCA and the False Claims Act. However, recent case law has called into question the extent to which government in the United States, including FDA, can, and is willing to seek to, prevent truthful and non-misleading speech related to off-label uses of FDA-approved products such as Vascepa.

In May 2015, we and a group of independent physicians filed a lawsuit against the FDA seeking a federal court declaration that would permit us and our agents to promote to healthcare professionals the use of Vascepa in the ANCHOR population and promote on the potential of Vascepa to reduce the risk of cardiovascular disease so long as the promotion is truthful and non-misleading. This use of Vascepa at issue reflected recognized medical practice but was not approved by the FDA and is thus not covered by current FDA-approved labeling for the drug. Promotion of an off-label use has generally been considered by the FDA to be illegal under the FDCA. The lawsuit, captioned *Amarin Pharma, Inc., et al. v. Food & Drug Administration, et al.*, 119 F. Supp. 3d 196 (S.D.N.Y. 2015), was filed in the United States District Court for the Southern District of New York. In the lawsuit, we contended principally that FDA regulations limiting off-label promotion of truthful and non-misleading information are unconstitutional under

the freedom of speech clause of the First Amendment to the U.S. Constitution as applied in the case of our proposed promotion of Vascepa. The physicians in the suit regularly treated patients at risk of cardiovascular disease and, as the complaint contended, have First Amendment rights to receive truthful and non-misleading information from Amarin. The suit was based on the principle that better informed physicians make better treatment decisions for their patients. The FDA opposed this lawsuit but did not dispute the veracity of the subject ANCHOR clinical trial data (the safety data from which was already and currently is in FDA-approved labeling of Vascepa) or the peer-reviewed research related to Vascepa and the potential for cardiovascular risk reduction.

In connection with this litigation, the FDA sent a detailed letter to us on June 5, 2015 that confirmed the validity of the ANCHOR trial results. The letter also sought to clarify how, in the FDA's view, applicable law and FDA policies apply to the communications proposed in our complaint. The FDA stated in this letter that it did not have concerns with much of the information we proposed to communicate and provided us with guidance on the FDA's view of lawful, but limited paths for the dissemination and communication to healthcare professionals of the effects of Vascepa demonstrated in the ANCHOR clinical trial and use of peer-reviewed scientific publications in the context of appropriate disclaimers.

In August 2015, we were granted preliminary relief in this lawsuit through the court's declaratory judgment that confirmed we may engage in truthful and non-misleading speech promoting the off-label use of Vascepa to healthcare professionals, i.e., to treat patients with persistently high triglycerides, and that such speech may not form the basis of a misbranding action under the FDCA. In

August 2015, we began to communicate promotional information beyond the MARINE indication to healthcare professionals in the United States as permitted by this court declaration. The FDA did not appeal the court's ruling.

In March 2016, we settled this litigation under terms by which the FDA and the U.S. government agreed to be bound by the conclusions from the federal court order that we may engage in truthful and non-misleading speech promoting the off-label use of Vascepa and that certain statements and disclosures that we proposed to make to healthcare professionals were truthful and non-misleading. As part of the settlement, given, as expressed in the court's opinion, that the dynamic nature of science and medicine is that knowledge is ever-advancing and that a statement that is fair and balanced one day may become incomplete or otherwise misleading in the future as new studies are done and new data is acquired, we agreed that we bear the responsibility to ensure that our communications regarding off-label use of Vascepa remain truthful and non-misleading, consistent with the federal court ruling.

While we believe we are now permitted under our settlement and the freedom of speech clause of the First Amendment to the United States Constitution to more broadly promote Vascepa, the FDA-approved labeling for Vascepa did not change as a result of this litigation and settlement. In addition, under our settlement, neither government nor other third-party coverage or reimbursement to pay for the off-label use of Vascepa was required. Based on our communications with the FDA, we expect that the FDA's review and analysis of our final positive results from the REDUCE-IT outcomes study will be required for FDA-approved label expansion for Vascepa. However, we proactively communicate results from the REDUCE-IT trial in a manner we believe is truthful and non-misleading and thus protected under the freedom of speech clause of the First Amendment to the United States Constitution.

Even though we have the benefit of a final settlement in this litigation, our promotion is still subject to a high, perhaps abnormally high, degree of scrutiny to ensure that our promotion remains within the scope covered by the settlement. For example, under the settlement, we remain responsible for ensuring our speech is truthful and non-misleading. Data arising from studies of drug products are complex, such as the many studies that we believe show supportive but not conclusive research on the potential connection between the effects of EPA, the active ingredient in Vascepa, and cardiovascular risk reduction (e.g., the JELIS trial of a highly-pure EPA product in Japan by Mochida Pharmaceutical Co., Ltd., or Mochida, and other data using a variety of levels of evidence that connect EPA to favorable effects toward reduced cardiovascular risk). We, the FDA, the U.S. government, our competitors and other interested parties may not agree on the truthfulness and non-misleading nature of our promotional materials with respect to the outcome of these trials or other direct or indirect claims we make about Vascepa. Likewise, the FDA, the U.S. government, our competitors and other interested parties may not agree on the truthfulness and non-misleading nature of our promotional materials related to the REDUCE-IT results. Federal and state governments or agencies may also seek to find other means to prevent our promotion of unapproved truthful and non-misleading information about Vascepa. If our promotional activities or other operations are found to be in violation of any law or governmental regulation through existing or new interpretations, we may be subject to prolonged litigation, penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Also, if governmental parties or our competitors view our claims as misleading or false, we could also be subject to liability based on fair competition-based statutes, such as the Lanham Act. Any of such negative circumstances could adversely affect our ability to operate our business and our results of operations.

Foreign Regulation of New Drug Compounds

In addition to regulations in the United States, we may be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in all or most foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a

clinical trial application, or CTA, much like the IND prior to the commencement of human clinical trials. In Europe, for example, a CTA must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed. Similarly, clinical trials conducted in countries such as Australia, Canada, and New Zealand, require review and approval of clinical trial proposals by an ethics committee, which provides a combined ethical and scientific review process. Most countries in which clinical studies are conducted require the approval of the clinical trial proposals by both the regulatory body and ethics committee.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with GCP, which have their origin in the World Medical Association's Declaration of Helsinki, the applicable regulatory requirements, and guidelines developed by the International Conference on Harmonization, or ICH, for GCP practices in clinical trials.

Post-Marketing Requirements

Following approval of a new product, a pharmaceutical company generally must engage in numerous specific monitoring and recordkeeping activities, such as routine safety surveillance, and must continue to submit periodic and other reports to the applicable

regulatory agencies, including any cases of adverse events and appropriate quality control records. Such reports submitted to the FDA may result in changes to the label and/or other post-marketing requirements or actions, including product withdrawal. These are viable risks once a product is on the market. Additionally, modifications or enhancements to the products or labeling or changes of site of manufacture are often subject to the approval of the FDA and other regulators, which may or may not be received or may result in a lengthy review process.

Prescription drug advertising is subject to federal, state and foreign regulations. In the United States, the FDA regulates prescription drug promotion, including direct-to-consumer advertising. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Any distribution of prescription drug products and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or the PDMA, a part of the FDCA.

In the United States, once a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in specific approved facilities and in accordance with pharmaceutical cGMPs, and NDA holders must list their products and register their manufacturing establishments with the FDA. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMPs, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them.

Federal and State Fraud and Abuse Laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws restrict certain marketing practices in the biopharmaceutical industry. These laws include anti-kickback statutes and false claims statutes.

The federal anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for a referral or the purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any healthcare facility, item or service reimbursable under Medicare, Medicaid, or other federal healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. Liability may be established without a person or entity having actual knowledge of the federal anti-kickback statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants or patient or product support programs.

The federal civil False Claims Act prohibits, among other things, any person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of government funds, or knowingly making or using, or causing to be made or used, a false record or statement material to an obligation to pay money to the government or knowingly concealing, or knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. The False Claims Act also permits a private individual acting as a “whistleblower” to bring actions

on behalf of the federal government alleging violations of the statute and to share in any monetary recovery. Recently, several pharmaceutical and other healthcare companies have been investigated or faced enforcement actions under the federal civil False Claims Act for a variety of alleged improper marketing activities, including allegations that they caused false claims to be submitted because of the company's marketing of the product for unapproved, and thus allegedly non-reimbursable, uses. Federal enforcement agencies also have showed increased interest in pharmaceutical companies' product and patient assistance programs, including reimbursement and co-pay support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs.

The Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), collectively referred to herein as HIPAA, among other things, imposes criminal and civil liability for knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payor and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. In addition, HITECH imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information.

The federal Physician Payment Sunshine Act, being implemented as the Open Payments Program, which requires manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to direct or indirect payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held in the company by physicians and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives.

The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers. Other states or localities may have laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs; require drug manufacturers to report information related to clinical trials, or information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and/or require identification or licensing of sales representatives.

Because of the breadth of these laws and the narrowness of the exceptions or safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Such a challenge could have a material adverse effect on our business, financial condition and results of operations. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business.

If our promotional activities or other operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us through existing or new interpretations, we may be subject to prolonged litigation, penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Also, if governmental parties or our competitors view our claims as misleading or false, we could also be subject to liability based on fair competition-based statutes, such as the Lanham Act. Any of such negative circumstances could adversely affect our ability to operate our business and our results of operations.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs. The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any

reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payers. In addition, there has been renewed interest in amending the Social Security Act to allow Medicare to negotiate prices for prescription drugs covered under Medicare Part B. If this were to be enacted by Congress and signed by the President, the prices we obtain for our products covered under Part B could be lower than the prices we might otherwise obtain, and it could exert a similar lowering pressure on payments from non-governmental payers.

The Agency for Healthcare Research and Quality (AHRQ), established by the MMA and provided additional funding by The American Recovery and Reinvestment Act of 2009, conducts comparative effectiveness research on different treatments for the same illness. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payers, is it possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates. If third-party payers do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

In March 2010 the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers and significantly impacts the pharmaceutical industry. Among the provisions of the ACA of greatest importance to the pharmaceutical and biotechnology industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs, that began in 2011;
- a licensure framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending that began on January 1, 2011.

Some of the provisions of the ACA have yet to be fully implemented, and certain provisions have been subject to judicial and Congressional challenges. In addition, there have been efforts by the Trump administration to repeal or replace certain aspects of the ACA and to alter the implementation of the ACA and related laws. For example, the Tax Cuts and Jobs Act enacted on December 22, 2017, eliminated the tax-based shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code of 1986, commonly referred to as the “individual mandate,” effective January 1, 2019. Further, the Bipartisan Budget Act of 2018 among other things, amended the Medicare statute, effective January 1, 2019, to reduce the coverage gap in most Medicare drug plans, commonly known as the “donut hole,” by raising the manufacturer discount under the Medicare Part D coverage gap discount program to 70%. It is unclear how the ACA and its implementation, as well as efforts to repeal or replace, or invalidate, the ACA, or portions thereof, will affect our business. It is possible that the ACA will continue to exert pressure on pharmaceutical pricing, especially under the Medicare and Medicaid programs, and may also increase our regulatory burdens and operating costs. Additional legislative changes, regulatory changes, and judicial challenges related to the ACA remain possible.

Pharmaceutical Pricing and Reimbursement

Our ability to successfully commercialize our product depends in significant part on the availability of adequate financial coverage and reimbursement from third-party payors, including, in the United States, governmental payors such as Medicare and Medicaid, as well as managed care organizations, private health insurers and other organizations. Third-party payors decide which drugs they will pay for and establish reimbursement and copayment levels. Third-party payors are increasingly challenging the prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost effectiveness of our products. Even with studies, our products may be considered less safe, less effective or less cost effective than other products, and third-party payors may not provide coverage and reimbursement for our product candidates, in whole or in part.

Political, economic and regulatory influences are subjecting the healthcare industry in the United States to fundamental changes. There have been, and we expect there will continue to be, legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell our products profitably. We anticipate that the United States Congress, state legislatures and the private sector will continue to consider and may adopt healthcare policies intended to curb rising healthcare costs. These cost containment measures include: controls on government funded reimbursement for drugs; new or increased requirements to pay prescription drug rebates to government healthcare programs; controls on healthcare providers; challenges to the pricing of drugs or limits or prohibitions on reimbursement for specific products through other means; requirements to try less expensive products or generics before a more expensive branded product; changes in drug importation laws; expansion of use of managed care

systems in which healthcare providers contract to provide comprehensive healthcare for a fixed cost per person; and public funding for cost effectiveness research, which may be used by government and private third-party payors to make coverage and payment decisions. Further, federal budgetary concerns could result in the implementation of significant federal spending cuts, including cuts in Medicare and other health related spending in the near term. For example, beginning April 1, 2013, Medicare payments for all items and services, including drugs and biologics, were reduced by 2% under the sequestration (i.e., automatic spending reductions) required law and this reduction runs to 2027. These cuts reduce reimbursement payments related to our products, which could potentially negatively impact our revenue.

Payors also are increasingly considering new metrics as the basis for reimbursement rates, such as average sales price, average manufacturer price and Actual Acquisition Cost. CMS surveys and publishes retail community pharmacy acquisition cost information in the form of National Average Drug Acquisition Cost files to provide state Medicaid agencies with a basis of comparison for their own reimbursement and pricing methodologies and rates. It is difficult to project the impact of these evolving reimbursement

mechanics on the willingness of payors to cover our products. We participate in the Medicaid Drug Rebate program, the 340B drug pricing program, and the U.S. Department of Veterans Affairs, or VA, Federal Supply Schedule, or FSS, pricing program. Under the Medicaid Drug Rebate program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Part B of the Medicare program.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the 340B drug pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and Medicaid rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, we participate in the VA/FSS pricing program. Under this program, we are obligated to make our products available for procurement on an FSS contract and charge a price to four federal agencies - the VA, U.S. Department of Defense, Public Health Service and U.S. Coast Guard - that is no higher than the statutory Federal Ceiling Price, or FCP. The FCP is based on the non-federal average manufacturer price, or Non-FAMP, which we calculate and report to the VA on a quarterly and annual basis. We also participate in the Tricare Retail Pharmacy program, under which we pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP.

The Medicaid Drug Rebate program, 340B program, and VA/FSS pricing program, and the risks relating to price reporting and other obligations under these programs, are further discussed under the heading "If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects" in Part I, Item 1A of this Annual Report on Form 10-K.

FDA Marketing Exclusivity and Generic Competition

The FDCA, as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, as amended, or the Hatch-Waxman Amendments, provides for market exclusivity provisions that can help protect the exclusivity of new drugs by delaying the acceptance and final approval of certain competitive drug applications. NCE marketing exclusivity precludes approval during the five-year exclusivity period of certain 505(b)(2) applications and abbreviated new drug applications, or ANDAs, submitted by another company for another version of the drug. The timelines and conditions under the ANDA process that permit the start of patent litigation and allow the FDA to approve generic versions of brand name drugs like Vascepa differ based on whether a drug receives three-year, or five-year, NCE marketing exclusivity. In May 2016, after significant litigation, FDA determined that Vascepa is eligible for NCE marketing exclusivity. Accordingly, we believe a related 30-month stay is currently in place with respect to our 1-gram dose strength of Vascepa that is scheduled to continue until January 26, 2020, seven-and-a-half years from FDA approval of Vascepa, unless related patent litigation is resolved against us sooner.

The FDA typically makes a determination on marketing exclusivity in connection with an NDA approval of a drug for a new indication. FDA marketing exclusivity is separate from, and in addition to, patent protection, trade secrets and

manufacturing barriers to entry which could also help protect Vascepa against generic competition.

We applied to the FDA for five-year, NCE marketing exclusivity for Vascepa in connection with the NDA for our MARINE indication, which NDA was approved by the FDA on July 26, 2012. On February 21, 2014, in connection with the July 26, 2012 approval of the MARINE indication, the FDA denied a grant of five-year NCE marketing exclusivity to Vascepa and granted three-year marketing exclusivity. Under applicable regulations, such three-year exclusivity would have extended through July 25, 2015 and would have been supplemented by a 30-month stay triggered by patent litigation that would have extended into September 2016, unless such patent litigation was resolved against us sooner.

NCE marketing exclusivity precludes approval during the five-year exclusivity period of certain 505(b)(2) applications and ANDAs 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 such case, the pioneer drug company is afforded the benefit of a 30-month stay against the launch of such a competitive product that extends from the end of the five-year exclusivity period. A pioneer company could also be afforded extensions to the stay under applicable regulations, including a six-month pediatric exclusivity extension or a judicial extension if applicable requirements are met. A drug sponsor could also gain a form of marketing

exclusivity under the Hatch-Waxman Amendments if such company can, under certain circumstances, complete a human clinical trial process and obtain regulatory approval of its product.

In contrast, a three-year period of exclusivity under the Hatch-Waxman Amendments is generally granted for a drug product that contains an active moiety that has been previously approved, such as 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. Accordingly, we expect to receive three-year exclusivity in connection with any future regulatory approvals of Vascepa, such as an approval sought based on positive REDUCE-IT outcomes study results. Such three-year exclusivity protection precludes the FDA from approving a marketing application for an ANDA, 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. The FDA may accept and commence review of such applications during the three-year exclusivity period. Such three-year exclusivity grant does not prevent a company from challenging the validity of patents at any time, subject to any prior four-year period pending from a grant of five-year exclusivity. 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.

On February 27, 2014, we sued the FDA in the U.S. District Court for the District of Columbia to challenge the agency's denial of five-year NCE exclusivity for Vascepa, based on our reading of the relevant statute, our view of FDA's inconsistency with its past actions in this area and the retroactive effect of what we believe is a new policy at FDA as it relates to our situation. On May 28, 2015, the court granted our motion for summary judgment. The decision vacated the FDA's denial of our claim for such exclusivity and remanded to the FDA for proceedings consistent with the decision. On July 22, 2015, Watson Laboratories Inc., the purported first Vascepa ANDA filer, sought to intervene and appeal the court's decision. We and FDA opposed this intervention effort. The applicable courts denied Watson the relief sought and appeal periods have expired.

On May 31, 2016, in a reversal that FDA and we view as consistent with the court's May 28, 2015 summary judgment motion, FDA determined that Vascepa is eligible for five-year, NCE marketing exclusivity. We believe this determination provides Vascepa with the benefits of NCE exclusivity afforded by statute. NCE exclusivity for Vascepa ran from its date of FDA approval on July 26, 2012 and extended until July 26, 2017. We believe the statutory NCE-related 30-month stay triggered by the 1-gram dose patent litigation following generic application submissions permitted on July 26, 2016 is scheduled to continue until January 26, 2020, seven-and-a-half years from FDA approval, unless such patent litigation is resolved against us sooner.

It is possible, but unlikely at this time given the time remaining in the 30-month stay, that FDA's NCE determination and related 30-month stay could be challenged by interested parties. If challenged, we plan to vigorously defend exclusivity for Vascepa. Any such challenge could have a negative impact on our company and create uncertainty around the continued benefits associated with exclusivity that we believe are applicable to us under the Hatch-Waxman Amendments.

Regulatory exclusivity is in addition to exclusivity afforded by issued patents related to Vascepa.

Other Regulatory Matters

Manufacturing, sales, promotion, importation, and other activities related to approved products are also subject to regulation by numerous regulatory authorities, including, in the United States, the FDA, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency, and state and local governments. Sales,

marketing and scientific/educational programs must comply with the Food, Drug, and Cosmetic Act, the Anti-Kickback Statute, and the False Claims Act and similar state laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory 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 product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies 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. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations or statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Patents, Proprietary Technology, Trade Secrets

Our success depends in part on our ability to obtain and maintain intellectual property protection for our drug candidates, technology and know-how, and to operate without infringing the proprietary rights of others. Our ability to successfully implement our business plan and to protect our products with our intellectual property 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.

We have prosecuted, and are currently prosecuting, multiple patent applications to protect the intellectual property developed during the Vascepa development program. As of the date of this report, we had 79 patent applications in the United States that have been either issued or allowed and more than 30 additional patent applications are pending in the United States. Such 79 allowed and issued applications include the following:

- 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;
- 43 U.S. patents covering or related to the use of Vascepa in either the MARINE or ANCHOR populations that have terms that expire in 2030 or later;
- 11 U.S. patents covering or related to the use of Vascepa in the REDUCE-IT population with terms expiring in 2033 or later;
- 4 additional patents related to the use of a pharmaceutical composition comprised of free fatty acids to treat the ANCHOR patient population with a term that expires in 2030 or later;
- 2 additional patents related to the use of a pharmaceutical composition comprised of free fatty acids to treat the MARINE patient population with a term that expires in 2030;
- 3 additional patents related to the use of a pharmaceutical composition comprised of free fatty acids to treat the REDUCE-IT population expiring 2033;
- 1 additional patent related to a pharmaceutical composition comprised of free fatty acids and uses thereof to treat both the MARINE and ANCHOR patient populations with a term that expires in 2030;
- 1 additional patent related to the use of a pharmaceutical composition comprised of re-esterified EPA triglyceride to treat the REDUCE-IT population expiring 2033;
- 3 additional patents related to a formulation of EPA/DHA and uses thereof with a term that expires in 2030;
- 2 additional patents related to the use of Vascepa to treat obesity with a term that expires in 2034;
- 2 additional patents covering a pharmaceutical composition comprised of EPA and a hydroxyl compound with a term that expires in 2034; and
- 4 additional patents covering a new combination therapy comprised of EPA and another drug.

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 applications with issued notices of allowance will be issued as patents or that any of our pending patent applications will issue as patents. No assurance can be given that, if and when issued, our patents will prevent competitors from competing with Vascepa. For example, we may choose to not assert all issued patents in patent litigation and patents or claims within patents may be determined to be invalid.

We are the owner of the above-listed patents. We are also the exclusive licensee of certain patents owned by others covering products in development. To secure our debt under our outstanding royalty-like instrument, we have granted the holders of such instrument a security interest in our Vascepa-related patents.

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, including, for example, under our collaboration with Mochida. 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. For example, one of our patents was revoked in an opposition proceeding in Europe due to a determination of improper claim amendments under a provision of law not applicable in the United States. 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.

Employees

At February 22, 2019, we had 530 full-time employees employed in sales, marketing, general and administrative and research and development functions. We believe our relations with our employees are good.

Organizational Structure

At February 22, 2019, we had the following subsidiaries:

Subsidiary Name	Country of Incorporation	Proportion of Ownership Interest and
-----------------	-----------------------------	---

	or Registration	Voting Power Held
Amarin Pharmaceuticals Ireland Limited	Ireland	100%
Amarin Pharma Inc.	United States	100%
Amarin Neuroscience Limited	Scotland	100%
Corsicanto II DAC	Ireland	100%
Ester Neurosciences Limited	Israel	100%

As of the date of this Annual Report on Form 10-K, our principal operating activities were being conducted by Amarin Corporation plc, together with Amarin Pharmaceuticals Ireland Limited and Amarin Pharma, Inc., with little to no operating activity being conducted by Amarin Neuroscience Limited, Corsicanto II DAC, or Ester Neurosciences Limited. Corsicanto DAC (formerly Corsicanto Limited) was liquidated in January 2019 pursuant to a resolution of Amarin Corporation plc as a sole shareholder.

Available Information

Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, are made available free of charge on or through our website at www.amarincorp.com as soon as reasonably practicable after such reports are filed with, or furnished to, the Securities and Exchange Commission, or SEC. The SEC also maintains a website, www.sec.gov, that contains reports and other

information regarding issuers that file electronically with the SEC. We are not, however, including the information contained on our website, or information that may be accessed through links on our website, as part of, or incorporating such information by reference into, this Annual Report on Form 10-K.

Financial Information

The financial information required under this Item 1 is incorporated herein by reference to Item 8 of this Annual Report on Form 10-K.

Item 1A. Risk Factors

This Annual Report on Form 10-K contains forward-looking information based on our current expectations. Because our actual results may differ materially from any forward-looking statements that we make or that are made on our behalf, this section includes a discussion of important factors that could affect our actual future results, including, but not limited to, our ability to successfully commercialize Vascepa, our capital resources, the progress and timing of our clinical programs, the safety and efficacy of our product candidates, risks associated with regulatory filings, the potential clinical benefits and market potential of our product candidates, commercial market estimates, future development efforts, patent protection, effects of healthcare reform, reliance on third parties, effects of tax reform, and other risks set forth below.

Risks Related to the Commercialization and Development of Vascepa

We are substantially dependent upon sales of Vascepa in the United States.

As a result of our reliance on a single product, Vascepa® (icosapent ethyl) capsules, 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. If commercialization efforts for Vascepa do not meet expectations, our business could be materially and adversely affected.

Even if we are able to successfully develop Vascepa outside the United States or develop additional products from our research and development efforts, the development time cycle for products typically takes several years. If we seek to diversify our development programs or product offerings through licensing or acquisitions, such transactions are also time-consuming, dilutive to existing shareholdings, and can be disruptive to operations. These dynamics can restrict our ability to respond rapidly to adverse business conditions for Vascepa. If demand for Vascepa does not meet expectations and we are not successful with development, 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 markets and products we develop could constrain our ability to generate revenues and achieve profitability.

Factors out of our control make it more difficult for Vascepa to achieve a level of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

In January 2013, we launched Vascepa based on the U.S. Food and Drug Administration, or FDA, approval of our MARINE indication, for use as an adjunct to diet to reduce triglyceride levels in adult patients with severe (TG \geq 500 mg/dL) hypertriglyceridemia. Guidelines for the management of very high triglyceride levels suggest that the primary goal of reducing triglyceride levels in this patient population is reduction in the risk of acute pancreatitis. A secondary goal for this patient population is to reduce cardiovascular risk. The effect of Vascepa on cardiovascular mortality and morbidity, or the risk for pancreatitis, in patients with severe hypertriglyceridemia has not been determined and our

FDA-approved labeling and promotional efforts state these facts.

In August 2015, based on a federal court order, we began communicating promotional information beyond the MARINE indication to healthcare professionals in the United States for the treatment of patients with high (TG \geq 200 mg/dL and $<$ 500 mg/dL) triglyceride levels who are also on statin therapy for elevated low-density lipoprotein cholesterol, or LDL-C, levels, based on results from the ANCHOR study of Vascepa. Many patients with high triglycerides also have other lipid level abnormalities such as high cholesterol and are on statin therapy. FDA did not approve Vascepa for use in this population due to the uncertain effect of pharmaceutically induced triglyceride reduction in this patient population on cardiovascular risk reduction, the ultimate targeted clinical benefit. Our promotional efforts disclose this fact and what we view as truthful and non-misleading information on the current state of research on both triglyceride reduction and the active pharmaceutical ingredient, or API, in Vascepa, EPA, as each relate to the potential of Vascepa to reduce cardiovascular risk.

In September 2018, we announced topline results from the REDUCE-IT™ (Reduction of Cardiovascular Events with EPA—Intervention Trial) cardiovascular (CV) outcomes study of Vascepa. In November 2018, we announced the primary results of our REDUCE-IT cardiovascular outcomes study confirming 25% relative risk reduction for the topline primary endpoint result with multiple robust demonstrations of efficacy, including 20% reduction in cardiovascular death. REDUCE-IT was a multinational, prospective,

randomized, double-blind, placebo-controlled study, enrollment for which started in November 2011. REDUCE-IT investigated the effects of Vascepa on CV risk in statin-treated adults with well-controlled LDL-C 41-100 mg/dL (median baseline LDL-C: 75 mg/dL) and other CV risk factors, including persistent elevated TG 150-499 mg/dL (median baseline TG: 216 mg/dL). REDUCE-IT topline results showed the trial met its primary endpoint demonstrating an approximately 25% relative risk reduction, to a high degree of statistical significance ($p < 0.001$), in major adverse cardiovascular events (MACE) in the intent-to-treat patient population with use of Vascepa 4 grams/day as compared to placebo. MACE events were defined as a composite of cardiovascular death, nonfatal myocardial infarction (MI), nonfatal stroke, coronary revascularization, or unstable angina requiring hospitalization. This result was supported by robust demonstrations of efficacy across multiple secondary endpoints. Vascepa was well tolerated in REDUCE-IT with a safety profile generally consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labeling. The proportions of patients experiencing adverse events and serious adverse events in REDUCE-IT were similar between the active and placebo treatment groups. Based on the final positive results of REDUCE-IT, we plan to seek additional indicated uses for Vascepa in the United States and to continue to develop Vascepa commercially in major markets around the world.

Even though we have released positive results from the REDUCE-IT trial, our approved label for Vascepa in the United States currently remains unchanged pending additional interactions and review by the FDA. A failure to obtain an expanded label may make it more difficult for Vascepa to gain 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 product revenues sufficient to become profitable. The degree of market acceptance of Vascepa for the MARINE indication and in ANCHOR patients and in any future indications and uses based on the REDUCE-IT trial or otherwise will depend on a number of factors, including:

- the perceived efficacy and safety of Vascepa by prescribing healthcare professionals, as compared to no treatment and as compared to alternative treatments in various at-risk patient populations, both as studied in clinical trials of Vascepa such as MARINE, ANCHOR and REDUCE-IT and not studied but for which the benefit/risk profile may be viewed as positive;
- peer review of REDUCE-IT results and publication of results in one or more medical journals over time;
- the FDA's review and analysis of the results of REDUCE-IT;
- 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;
- publicity concerning Vascepa or competing products;
- our ability to continually promote Vascepa in the United States outside of FDA-approved labeling and the related perception thereof;
- sufficient third-party coverage or reimbursement for on-label use, and for permitted off-label use, the third-party coverage or reimbursement which was not addressed in the scope of the August 2015 court declaration or related settlement;
- natural disasters that can inhibit our ability to promote Vascepa regionally and can negatively affect product demand by creating obstacles for patients to seek treatment and fill prescriptions;
- new policies or laws affecting Vascepa sales, such as state and federal efforts to affect drug pricing and provide or remove healthcare coverage that includes reimbursement for prescription drugs; 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.

As with any cardiovascular outcomes trial, over time further REDUCE-IT data assessment and data release will yield additional useful information to inform greater understanding of study outcome. That additional data may exceed, meet or not meet investor expectations. If the additional data do not meet expectations, the perception of REDUCE-IT

results and Vascepa may suffer and our stock price may decline.

In September 2018, we announced topline results from the REDUCE-IT trial showing that the trial met its primary endpoint demonstrating an approximately 25% relative risk reduction, to a high degree of statistical significance ($p < 0.001$), in MACE in the intent-to-treat patient population with use of Vascepa 4 grams/day as compared to placebo. More detailed presentation of REDUCE-IT results was first made at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018 with such results concurrently published in The New England Journal of Medicine. Additional data assessment and data release will yield additional useful information to inform greater understanding of study outcome. Generally, trial data assessment sufficient to convey a complete picture of trial data typically takes several months and can take years to complete and publish. When new data are assessed and released it could exceed, match or may not meet investor expectations. For example, a presentation of additional analyses of

REDUCE-IT results is scheduled for the American College of Cardiology (ACC) 2019 Scientific Sessions on March 18, 2019 in New Orleans, Louisiana. This presentation and additional data may exceed, match or may not meet investor expectations.

In addition, the same set of data can sometime be interpreted to reach conclusions that conflict with our conclusions, as was the case when FDA reviewed earlier cardiovascular outcomes trials of other drugs in the context of the effects of triglyceride lowering agents on cardiovascular risk reduction.

Aspects that could change and impact the final evaluation of the totality of the efficacy and safety data from REDUCE-IT may include some or all of the following:

- the magnitude of the treatment benefit on the primary composite endpoint, its components, secondary endpoints and the primary and secondary risk prevention cohorts;
- consideration of which components of the composite or secondary endpoints have the most clinical significance;
- the consistency of the primary and secondary outcomes;
- the consistency of findings across cohorts and important subgroups;
- safety considerations and risk/benefit considerations;
- consideration of REDUCE-IT results in the context of other clinical studies;
- consideration of the cumulative effect of Vascepa in studied patients; and
- study conduct and data quality, integrity and consistency.

If release of additional data do not meet expectations, the perception of REDUCE-IT results and the perceived value of Vascepa may suffer. If this occurs our business could suffer and our stock price could significantly decline.

Clinical trials that we or potential partners conduct, including the REDUCE-IT trial, may not provide sufficient safety and efficacy data to obtain the requisite regulatory approvals for product candidates or to achieve a level of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success if we obtain regulatory approval.

On November 10, 2018, we announced the primary results of our REDUCE-IT cardiovascular outcomes study confirming 25% relative risk reduction for the topline primary endpoint result with multiple robust demonstrations of efficacy, including 20% reduction in cardiovascular death. Major cardiovascular outcomes studies like REDUCE-IT typically motivate the medical community to search for ways to fit the results into the mosaic of prior studies considered as successful, like JELIS, and CANTOS, and their associated mechanisms of action, and to also distinguish results from prior failed studies, like what the authors of The New England Journal of Medicine editorial on REDUCE-IT referred to as the “parade of failed cardiovascular outcome trials of fish oils.” It is important for the medical community to understand related science on the unique active pharmaceutical ingredient in Vascepa, icosapent ethyl, and REDUCE-IT. As with any clinical study, as the medical community and regulators such as the FDA review and analyze REDUCE-IT study data, dialogue is expected to continue with respect to the reliability of REDUCE-IT data and the study quality that could adversely affect our product development, regulatory review, market or medical community acceptance, and level of payor reimbursement in the event of an expansion of the Vascepa label. Likewise, public perception of the REDUCE-IT results and Vascepa may be affected.

For example, in the REDUCE-IT trial, cardiovascular benefits appeared not to be influenced significantly by TG levels at baseline (above or below 150 mg/dL baseline range) or as achieved at one year, potentially suggesting mechanisms at work with use of Vascepa that are independent of baseline TG levels or therapy-driven reduction in TG

levels. Determination of the mechanisms responsible for the benefit shown in REDUCE-IT was not the focus or purpose of the study. As summarized from the primary results of REDUCE-IT in *The New England Journal of Medicine*, potential Vascepa mechanisms of action at work in REDUCE-IT may include TG reduction, anti-thrombotic effects, antiplatelet or anticoagulant effects, membrane-stabilizing effects, effects on stabilization and/or regression of coronary plaque and inflammation reduction, each as supported by earlier stage mechanistic studies.

In addition, the median change in LDL cholesterol level from baseline was 6.6% (5.0 mg/dL; $p < 0.001$) on a placebo-corrected basis reflecting an increase of 3.1% (+2.0 mg/dL) in the Vascepa group and an increase of 10.2% (+7.0 mg/dL) in the placebo group. Increases in the placebo group relative to the Vascepa group were also observed in other parameters classically measured in such studies but with uncertain relevance to cardiovascular outcomes. An upward drift in LDL cholesterol and such other parameter has been commonly, although not always, observed in statin-stabilized patients across numerous studies within varying patient populations, and many have estimated LDL cholesterol increases of at least 6% and ranging up to more than 30%. Factors

cited as potentially contributing to this circumstance include decreased drug and lifestyle regimen compliance, physiological compensation for drug-induced lipid changes, regression to the mean, intraindividual variability, lab variability, genetics, metabolic state, disease state, age, and season. If light liquid paraffin oil, or mineral oil, used as the placebo in REDUCE-IT adversely affected statin absorption or other parameters in some patients as is asserted by certain critics of the study, this could be theorized to have contributed to differences in outcomes between the groups and leave open the possibility that the placebo used in the trial was not biologically inert. These and other observations, whether scientifically reliable or not, may negatively impact how these trial results are interpreted by regulators, the medical community and third-party payors. This is the case notwithstanding that a post hoc analysis of REDUCE-IT data published in The New England Journal of Medicine showed no material differences in the primary and key secondary endpoint event rates for placebo patients with an increase in LDL-C at one year versus those with no change or a decrease, and also suggested a similar relative risk reduction regardless of whether there was an increase in LDL cholesterol level among the patients in the placebo group. Data generated by Amarin after, but supporting, this analysis reflect that patient-by-patient differences in LDL cholesterol levels from baseline to Year 1 included some patients with increases, some patients with decreases and others with no change in both the Vascepa arm and the placebo arm of the REDUCE-IT study. If mineral oil affected statin absorption significantly, it is reasonable to expect that such effect might be evident in all patients on placebo (i.e., if mineral oil had a definitive effect one would expect LDL cholesterol increases would be consistently observed among patients in the placebo arm) rather than the observed mixed results that include many patients with LDL cholesterol decreases or lack of change in LDL cholesterol. Moreover, as the authors of the primary results publication on REDUCE-IT in The New England Journal of Medicine noted, the relatively small differences in LDL cholesterol levels between the groups would not be likely to explain the 25% lower MACE risk observed with Vascepa and JELIS, an over 18,000 patient cardiovascular outcomes study in Japan of a highly-pure EPA product similar to Vascepa, that, previously demonstrated a 19% risk reduction without a mineral oil placebo.

Consistent with our SPA for REDUCE-IT agreed to with the FDA, the trial subjects in the placebo arm of REDUCE-IT were given light liquid paraffin oil, or mineral oil, to mimic the color and consistency of Vascepa. We also used mineral oil in the placebo arms of our MARINE and ANCHOR trials. During the public advisory committee meeting held by FDA as part of its review of our ANCHOR sNDA, a discussion regarding observed, nominally statistically significant changes from baseline in an adverse direction, while on background statin therapy, in certain lipid parameters, including triglycerides, in the placebo group, led to further discussion about the possibility that the mineral oil placebo used in the ANCHOR trial (and in the REDUCE-IT trial) might not be biologically inert and might be viewed as artificially exaggerating the clinical effect of Vascepa when measured against placebo in the ANCHOR trial. Ultimately, no strong evidence for biological activity of mineral oil was identified by the FDA before its approval of Vascepa after review of the MARINE and ANCHOR trials and consideration of other data regarding mineral oil. The FDA, early in the course of the REDUCE-IT trial, directed the independent data monitoring committee, or DMC, for REDUCE-IT to periodically review unblinded lipid data to monitor for signals that the placebo might not be inert. After each such quarterly unblinded safety analysis and review meeting to date, the DMC recommended to continue the REDUCE-IT study as planned. Each of these DMC recommendations has been shared with FDA. In addition, following discussions on this topic in October 2013 in connection with the FDA's review of our supplemental new drug application for our ANCHOR study, the FDA did not seek to require that we include any qualification related to the use of mineral oil as a placebo in REDUCE-IT at the time of our March 2016 amendment to the REDUCE-IT SPA. As noted, importantly and consistently, JELIS, an over 18,000 patient cardiovascular outcomes study in Japan of a highly-pure EPA product similar to Vascepa previously demonstrated a 19% risk reduction without a mineral oil placebo.

As with any cardiovascular outcomes trial, further REDUCE-IT data assessment and data release could yield additional useful information to inform a greater understanding of the trial outcome. Further detailed data assessment by Amarin and regulatory authorities will continue and take several months or more to complete and record. The final evaluation of the totality of the efficacy and safety data from REDUCE-IT may include some or all of the following,

as well as other considerations: new information affecting the degree of treatment benefit on studied endpoints; study conduct and data robustness, quality, integrity and consistency; additional safety data considerations and risk/benefit considerations; consideration of the cumulative effect of Vascepa in studied patients; and consideration of REDUCE-IT results in the context of other clinical studies. That additional data may exceed, meet or not meet the expectations of regulators, the medical community and third-party payors.

If Vascepa's specific mechanism of action shown in the REDUCE-IT study or the potential effects of the mineral oil used in the placebo arm of REDUCE-IT remains uncertain, or any additional data from the REDUCE-IT study do not meet expectations, the perception of REDUCE-IT results and Vascepa may suffer and could adversely affect our product development, regulatory review, market or medical community acceptance, level of payor reimbursement in the event of an expansion of the Vascepa label, or the public perception of the REDUCE-IT results and Vascepa, any of which could have a material adverse effect on our business and financial condition and our stock price may decline.

Our current and planned commercialization efforts in the United States may not be successful in increasing sales of Vascepa.

Prior to REDUCE-IT topline results announcement in September 2018, our sales team consisted of approximately 170 sales professionals, including sales representatives and their managers. We have recently increased the size of our sales force to approximately 440 sales professionals, including approximately 400 sales representatives, pursuant to positive REDUCE-IT results

and are expanding our promotion of Vascepa. This sales team promotes Vascepa to a limited group of physicians and other healthcare professionals in select geographies in the United States. Even after planned expansion, this sales team is not large enough to call upon all physicians. We intend to further expand the promotion of Vascepa following our assumed label expansion for Vascepa, subject to FDA review and approval of our sNDA.

In May 2014, we began co-promoting Vascepa in the United States with Kowa Pharmaceuticals America, Inc. under a co-promotion agreement we entered into in March 2014, which we amended in July 2017. Under the agreement, Kowa Pharmaceuticals America, Inc. co-promoted Vascepa in conjunction with its promotion of its primary product, a branded statin for patients with high cholesterol, along with our sales professionals based on a plan designed to focus on select sales territories that we believed had demonstrated the greatest potential for Vascepa sales growth, increasing both the number of sales targets reached and the frequency of sales calls on existing sales targets. However, the commercialization of pharmaceutical products is a complex undertaking, and we had very limited experience as a company operating in this area and co-promoting a pharmaceutical product with a partner.

Furthermore, our agreement with Kowa Pharmaceuticals America, Inc. was designed such that Kowa's co-promotion of Vascepa ceased at the end of 2018. The parties mutually agreed not to renew the agreement. If our newly expanded sales team are not at least equally capable, our sales may be negatively impacted.

In addition to sales force expansion in the United States, Amarin plans to work with its international partners to support regulatory efforts outside the United States based on REDUCE-IT results. We will again need to overcome challenges associated with rapidly hiring and training personnel and managing larger teams of people.

Factors related to building and managing a sales and marketing organization that can inhibit our efforts to successfully commercialize Vascepa 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 the court declaration that we believe enables us to expand marketing efforts for Vascepa, 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;
- an inability by us or our partners to obtain regulatory and marketing approval or establish marketing channels in foreign jurisdictions; and
- unforeseen costs and expenses associated with operating a new independent sales and marketing organization.

If we are not successful in our efforts to market and sell Vascepa, our anticipated revenues will be materially and negatively affected, and we may not obtain profitability, may need to cut back on research and development activities or need to raise additional funding that could result in substantial dilution.

Our past and future off-label promotion of Vascepa could subject us to additional regulatory scrutiny and present unforeseen risks.

The Federal Food, Drug, and Cosmetic Act, or FDCA, has been interpreted by the FDA and the U.S. government to make it illegal for pharmaceutical companies to promote their FDA approved products for uses that have not been approved by the FDA. Companies that market drugs for off-label uses or indications have been subject to related costly litigation, criminal penalties and civil liability under the FDCA and the False Claims Act. However, recent case law has called into question the extent to which government in the United States, including FDA, can, and is willing to

seek to, prevent truthful and non-misleading speech related to off-label uses of FDA-approved products such as Vascepa.

In May 2015, we and a group of independent physicians filed a lawsuit against the FDA seeking a federal court declaration that would permit us and our agents to promote to healthcare professionals the use of Vascepa in the ANCHOR population and promote on the potential of Vascepa to reduce the risk of cardiovascular disease so long as the promotion is truthful and non-misleading. This use of Vascepa at issue reflected recognized medical practice but was not approved by the FDA and is thus not covered by current FDA-approved labeling for the drug. Promotion of an off-label use has generally been considered by the FDA to be illegal under the FDCA. The lawsuit, captioned Amarin Pharma, Inc., et al. v. Food & Drug Administration, et al., 119 F. Supp. 3d 196 (S.D.N.Y. 2015), was filed in the United States District Court for the Southern District of New York. In the lawsuit, we contended principally that FDA regulations limiting off-label promotion of truthful and non-misleading information are unconstitutional under the freedom of speech

clause of the First Amendment to the U.S. Constitution as applied in the case of our proposed promotion of Vascepa. The physicians in the suit regularly treated patients at risk of cardiovascular disease and, as the complaint contended, have First Amendment rights to receive truthful and non-misleading information from Amarin. The suit was based on the principle that better informed physicians make better treatment decisions for their patients. The FDA opposed this lawsuit but did not dispute the veracity of the subject ANCHOR clinical trial data (the safety data from which was already and currently is in FDA-approved labeling of Vascepa) or the peer-reviewed research related to Vascepa and the potential for cardiovascular risk reduction.

In August 2015, we were granted preliminary relief in this lawsuit through the court's declaratory judgment that confirmed we may engage in truthful and non-misleading speech promoting the off-label use of Vascepa to healthcare professionals, i.e., to treat patients with persistently high triglycerides, and that such speech may not form the basis of a misbranding action under the FDCA. In August 2015, we began to communicate promotional information beyond the MARINE indication to healthcare professionals in the United States as permitted by this court declaration. The FDA did not appeal the court's ruling.

In March 2016, we settled this litigation under terms by which the FDA and the U.S. government agreed to be bound by the conclusions from the federal court order that we may engage in truthful and non-misleading speech promoting the off-label use of Vascepa and that certain statements and disclosures that we proposed to make to healthcare professionals were truthful and non-misleading. As part of the settlement, given, as expressed in the court's opinion, that the dynamic nature of science and medicine is that knowledge is ever-advancing and that a statement that is fair and balanced one day may become incomplete or otherwise misleading in the future as new studies are done and new data is acquired, we agreed that we bear the responsibility to ensure that our communications regarding off-label use of Vascepa remain truthful and non-misleading, consistent with the federal court ruling.

While we believe we are now permitted under applicable law to more broadly promote Vascepa, the FDA-approved labeling for Vascepa did not change as a result of this litigation and settlement, and neither government nor other third-party coverage or reimbursement to pay for the off-label use of Vascepa promoted under the court declaration was required. Based on our communications with the FDA, we expect that the FDA's review and analysis of our final positive results from the REDUCE-IT outcomes study will be required for FDA-approved label expansion for Vascepa. However, we proactively communicate results from the REDUCE-IT trial in a manner we believe is truthful and non-misleading and thus protected under the freedom of speech clause of the First Amendment to the United States Constitution.

Even though we have the benefit of a final settlement in this litigation, our promotion is still subject to a high, perhaps abnormally high, degree of scrutiny to ensure that our promotion remains within the scope covered by the settlement. For example, under the settlement, we remain responsible for ensuring our speech is truthful and non-misleading. Data arising from studies of drug products are complex, such as the many studies that we believe show supportive but not conclusive research on the potential connection between the effects of EPA, the active ingredient in Vascepa, and cardiovascular risk reduction (e.g., the JELIS trial of a highly-pure EPA product in Japan by Mochida Pharmaceutical Co., Ltd., or Mochida, and other data using a variety of levels of evidence that connect EPA to favorable effects toward reduced cardiovascular risk). We, the FDA, the U.S. government, our competitors and other interested parties may not agree on the truthfulness and non-misleading nature of our promotional materials with respect to the outcome of these trials or other direct or indirect claims we make about Vascepa. Likewise, the FDA, the U.S. government, our competitors and other interested parties may not agree on the truthfulness and non-misleading nature of our promotional materials related to the REDUCE-IT results. Federal and state governments or agencies may also seek to find other means to prevent our promotion of unapproved truthful and non-misleading information about Vascepa. If our promotional activities or other operations are found to be in violation of any law or governmental regulation through existing or new interpretations, we may be subject to prolonged litigation, penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Also, if governmental parties

or our competitors view our claims as misleading or false, we could also be subject to liability based on fair competition-based statutes, such as the Lanham Act. Any of such negative circumstances could adversely affect our ability to operate our business and our results of operations.

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

The biotechnology and pharmaceutical industries are highly competitive. There are many pharmaceutical companies, biotechnology companies, public and private universities and research organizations actively engaged in the research and development of products that may be similar to our products. It is probable that the number of companies seeking to develop products and therapies similar to our products will increase. Many of these and other existing or potential competitors have substantially greater financial, technical and human resources than we do and may be better equipped to develop, manufacture and market products. These companies may develop and introduce products and processes competitive with or superior to ours. In addition, other technologies or products may be developed that have an entirely different approach or means of accomplishing the intended purposes of our products, which might render our technology and products noncompetitive or obsolete.

Our competitors both in the United States and abroad include large, well-established pharmaceutical and generic companies, specialty and generic pharmaceutical sales and marketing companies, and specialized cardiovascular treatment companies. GlaxoSmithKline plc currently sells Lovaza[®], a prescription-only omega-3 fatty acid indicated for patients with severe hypertriglyceridemia, which was approved by FDA in 2004 and has been on the market in the United States since 2005. Multiple

generic versions of Lovaza are available in the United States. Other large companies with competitive products include AbbVie, Inc., which currently sells Tricor[®] and Trilipix[®] for the treatment of severe hypertriglyceridemia and Niaspan[®], which is primarily used to raise high-density lipoprotein cholesterol, or HDL-C, but is also used to lower triglycerides. Multiple generic versions of Tricor, Trilipix and Niaspan are also available in the United States. We compete with these drugs, and in particular, multiple low-cost generic versions of these drugs, in our FDA-approved indicated use and in off-label uses, such as to beneficially affect lipid levels in patients with persistent high triglyceride levels after statin therapy with the aim of potentially lowering cardiovascular risk beyond statin therapy.

In addition, in May 2014, Epanova[®] (omega-3-carboxylic acids) capsules, a free fatty acid form of omega-3 (comprised of 55% EPA and 20% DHA), was approved by the FDA for patients with severe hypertriglyceridemia. Epanova was developed by Omthera Pharmaceuticals, Inc., and is now owned by AstraZeneca Pharmaceuticals LP (AstraZeneca). Also, in April 2014, Omtryg, another omega-3-acid fatty acid composition developed by Trygg Pharma AS, received FDA approval for severe hypertriglyceridemia. Neither Epanova nor Omtryg have been commercially launched, but could launch at any time. Each of these competitors, other than potentially Trygg, has greater resources than we do, including financial, product development, marketing, personnel and other resources. Neither Epanova or Omtryg have been commercially launched.

AstraZeneca is currently conducting a long-term outcomes study to assess Statin Residual Risk Reduction With EpaNova in HiGH Cardiovascular Risk PatientS With Hypertriglyceridemia (STRENGTH). The study is a randomized, double-blind, placebo-controlled (corn oil), parallel group design that is believed to have enrolled approximately 13,000 patients with hypertriglyceridemia and low HDL and high risk for cardiovascular disease randomized 1:1 to either corn oil plus statin or Epanova plus statin, once daily, for approximately 3-5 years as determined when the number of major adverse cardiovascular event outcomes is reached. The STRENGTH study is estimated to be completed in 2020, but it could be stopped earlier if, for example, it generates an overwhelming efficacy result. In addition, in March 2017, Kowa Research Institute (a subsidiary of the Japanese company Kowa Co., Ltd) initiated a phase III cardiovascular outcomes trial titled PROMINENT examining the effect of pemafibrate (experimental name K-877) in reducing cardiovascular events in Type II diabetic patients with hypertriglyceridemia. Kowa Research Institute has publicly estimated study completion in May 2022, and if successful, U.S. regulatory approval is estimated in mid-2023.

During 2018, two outcomes studies were completed of omega-3 mixtures which both failed to achieve their primary endpoints of cardiovascular risk reduction and two meta-analyses were published showing that omega-3 mixtures are not effective in lowering cardiovascular risk. Results of these failed outcomes studies and analysis, while not done with Vascepa, may negatively affect sales of Vascepa. For example, results of VITamin D and Omega-3 TriaL (VITAL), as announced immediately before the presentation of REDUCE-IT results at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018, failed to achieve its primary endpoint of lowering cardiovascular events. VITAL was an NIH funded randomized double-blind, placebo-controlled, 2x2 factorial trial of 2000 IU per day of vitamin D3 and 1 gram per day of omega-3 fatty acid supplementation (Lovaza) for the primary prevention of cancer and cardiovascular disease in a nationwide USA cohort of 25,874 adults not selected for elevated cardiovascular or cancer risk.

Likewise, in 2018, results from A Study of Cardiovascular Events iN Diabetes (ASCEND) trial were released and showed negligible results for omega-3 fatty acids 1 gram daily. ASCEND was a British Heart Foundation funded 2x2 factorial design, randomized study to assess whether aspirin 100 mg daily versus placebo and separately, omega-3 fatty acids 1 gram daily versus placebo, reduce the risk of cardiovascular events in a nationwide UK cohort of over 15,000 individuals with diabetes who do not have atherosclerotic cardiovascular disease. In addition, VITAL showed that supplementation with either omega-3 fatty acid at a dose of 1 gram per day or vitamin D3 at a dose of 2000 IU per day was not effective for primary prevention of CV or cancer events among healthy middle-aged men and women across 5 years of follow up.

In meta-analysis, presented in 2018 by the Cochran Foundation and separately as published in JAMA, additional omega-3 studies were evaluated. Similar to the VITAL and ASCEND studies, most of the studies in these omega-3 meta-analyses were of omega-3 mixtures, including DHA, and most were studies of relatively low doses of omega-3 as is associated with dietary supplementation and/or they studied relatively low risk patient populations. The exception was the JELIS study, conducted in Japan, of highly pure EPA which demonstrated a positive outcome benefit. The negative results from such omega-3 mixture studies could create misleading impressions about the use of omega-3s generally, including Vascepa, despite REDUCE-IT positive results and the highly-pure and stable EPA active ingredient in Vascepa and its higher dose regimen.

We are also aware of other pharmaceutical companies that are developing products that, if successfully developed, approved and marketed, would compete with Vascepa. Acasti Pharma, or Acasti, a subsidiary of Neptune Technologies & Bioresources Inc., announced in December 2015 that it intends to pursue a regulatory pathway under section 505(b)(2) of the FDCA for its omega-3 prescription drug candidate, CaPre[®] (omega-3 phospholipid), derived from krill oil, for the treatment of hypertriglyceridemia. In September 2016, Acasti announced positive results from its pivotal bioavailability bridging study comparing CaPre to Lovaza, establishing a scientific bridge between the two that is expected to support the feasibility of a 505(b)(2) regulatory pathway. Acasti initiated a Phase 3 clinical program (TRILOGY) to assess the safety and efficacy of CaPre in patients with very high (≥ 500 mg/dL)

triglycerides in the first quarter of 2018. Acasti completed enrollment in Q4 2018 and study completion is expected by the end of 2019. We believe Micelle BioPharma Inc., or Micelle, is also developing potential treatments for hypertriglyceridemia based on omega-3 fatty acids. To our knowledge, Micelle, after acquiring SC401 from Sancilio & Company, or Sancilio, is pursuing a regulatory pathway under section 505(b)(2) of the FDCA for its product and submitted an Investigational New Drug Application, or IND, in July 2015. Micelle (Sancilio) completed two pharmacokinetic studies and Phase 2 bioavailability studies (FASTR I&II), with one comparing SC401 to Lovaza. We expect the company or a potential partner to initiate a pivotal clinical Phase 3 study as the next step in development.

Matinas BioPharma, Inc. is developing an omega-3-based therapeutic (MAT9001) for the treatment of severe hypertriglyceridemia and mixed dyslipidemia. In the fourth quarter of 2014, Matinas BioPharma, Inc. filed an IND with the FDA to conduct a human study in the treatment of severe hypertriglyceridemia and, in June 2015, the company announced topline results for its head-to-head comparative pharmacokinetic and pharmacodynamic study of MAT9001 versus Vascepa in patients under conditions inconsistent with the FDA-approved label for Vascepa and presented results based on biomarker modification without outcomes data. In September 2017, Matinas announced that it will be seeking a partner company to develop and commercialize MAT9001. Akcea Therapeutics/Ionis Pharmaceuticals (formerly Isis Pharmaceuticals), or Akcea/Ionis, in August 2018 announced the receipt of a complete response letter from the FDA for WAYLIVRA™ (volanesorsen), a drug candidate administered through weekly subcutaneous injections, for the treatment of familial chylomicronemia syndrome (FCS). Akcea will continue to work with the FDA on the path forward for Waylivra for the treatment of FCS. Waylivra continues to be developed for the treatment of familial partial lipodystrophy (FPL).

A Phase 3 trial is currently ongoing studying Waylivra (volanesorsen) in patients with FPL (BROADEN trial). Akcea/Ionis expects to file an NDA for FPL in 2019. In January 2017, Akcea/Ionis announced a strategic collaboration and option agreement with Novartis whereby Novartis will help develop (including funding cardiovascular outcomes studies) and commercialize products emerging from this collaboration, including Waylivra (volanesorsen). In June 2018, Gemphire Therapeutics announced positive topline results from a Phase 2b trial (INDIGO-1) of its drug candidate, gemcabene, in patients with severe hypertriglyceridemia. Gemcabene is an oral, once-daily pill for a number of hypercholesterolemic populations and severe hypertriglyceridemia. Gemphire announced plans to initiate a Phase III study for homozygous familial hypercholesterolemia (HoFH), heterozygous familial hypercholesterolemia (HeFH) and non-familial hypercholesterolemia in ASCVD patients in the second half of 2018. In August 2018, the FDA requested that Gemphire conduct an additional long-term toxicity study before commencing any further clinical testing, thereby effectively placing gemcabene on clinical hold. Zydus Cadila has a Phase 2 development program for its lead molecule, Saroglitazar, in various indications, including severe hypertriglyceridemia in the United States. In August 2018, the company announced that it had suspended the Phase 2 trial in the severe hypertriglyceridemia indication due to study enrollment issues, while it continues development activities in other indications. The product is approved in India under the name Lipaglyn® for the treatment of hypertriglyceridemia and diabetic dyslipidemia. We are also aware that bezafibrate has been licensed by Intercept Pharmaceuticals to be further developed and potentially launched in the United States market.

Based on prior communications from the FDA, including communications in connection with its review of the ANCHOR indication for Vascepa, it is our understanding that the FDA is not prepared to approve any therapy for treatment of cardiovascular risk based on biomarker modification without outcomes study data, with the potential exception of therapies which lower LDL-cholesterol. In particular, it is our understanding that the FDA is not prepared to approve any therapy based on data demonstrating lowering of triglyceride levels. In our view, this position from the FDA is unlikely to change based on the REDUCE-IT study particularly in light of the independence of the positive benefit demonstrated in the REDUCE-IT study from triglyceride levels and benefit from the REDUCE-IT study supporting that the positive effects of Vascepa are unique to Vascepa and extend beyond triglyceride reduction. If the FDA were to change this position, it could potentially have a negative impact on Amarin by making it easier for other products to achieve a cardiovascular risk reduction indication without the need in advance to conduct a long and

expensive cardiovascular outcomes study.

Generic company competitors are seeking FDA approval of generic versions of Vascepa. We are now engaged in related patent litigation and could face other challenges to our exclusivity.

The FDCA, as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, as amended, or the Hatch-Waxman Amendments, permits the FDA to approve ANDAs for generic versions of brand name drugs like Vascepa. We refer to the process of generic drug applications as the “ANDA process.” The ANDA process permits competitor companies to obtain marketing approval for a drug product with the same active ingredient, dosage form, strength, route of administration, and labeling as the approved brand name drug, but without having to conduct and submit clinical studies to establish the safety and efficacy of the proposed generic product. In place of such clinical studies, an ANDA applicant needs to submit data demonstrating that its product is bioequivalent to the brand name product, usually based on pharmacokinetic studies.

As an alternate path to FDA approval for modifications of products previously approved by the FDA, an applicant may submit a new drug application, or NDA, under Section 505(b)(2) of the FDCA (enacted as part of the Hatch-Waxman Amendments). This

statutory provision permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference from the owner of the data. The Hatch-Waxman Amendments permit the applicant to rely upon the FDA findings of safety and effectiveness of a drug that has obtained FDA approval based on preclinical or clinical studies conducted by others. In addition to relying on FDA prior findings of safety and effectiveness for a referenced drug product, the FDA may require companies to perform additional preclinical or clinical studies to support approval of the modification to the referenced product.

If an application for a generic version of a branded product or a Section 505(b)(2) application relies on a prior FDA finding of safety and effectiveness of a previously-approved product including an alternative strength thereof, the applicant is required to certify to the FDA concerning any patents listed for the referenced product in the FDA publication called "Approved Drug Products with Therapeutic Equivalence Evaluations," otherwise known as the "Orange Book." Specifically, the applicant must certify in the application that:

- (I) there is no patent information listed for the reference drug;
- (II) the listed patent has expired for the reference drug;
- (III) the listed patent for the reference drug has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- (IV) the listed patent for the reference drug is invalid, unenforceable, or will not be infringed by the manufacture, use or sale of the product for which the ANDA or 505(b)(2) NDA is submitted.

The Hatch-Waxman Amendments require an applicant for a drug product that relies, in whole or in part, on the FDA's prior approval of Vascepa, to notify us of its application, a "paragraph IV" notice, if the applicant is seeking to market its product prior to the expiration of the patents that both claim Vascepa and are listed in the Orange Book. A bona fide paragraph IV notice may not be given under the Hatch-Waxman Amendments until after the generic company receives from the FDA an acknowledgement letter stating that its ANDA is sufficiently complete to permit a substantive review.

The paragraph IV notice is required to contain a detailed factual and legal statement explaining the basis for the applicant's opinion that the proposed product does not infringe our patents, that the relevant patents are invalid, or both. After receipt of a valid notice, the branded product manufacturer has the option of bringing a patent infringement suit in federal district court against any generic company seeking approval for its product within 45 days from the date of receipt of each notice. If such a suit is commenced within this 45-day period, the Hatch-Waxman Amendments provide for a 30-month stay on FDA's ability to give final approval to the proposed generic product, which period begins on the date the paragraph IV notice is received. Generally, during a period of time in which generic applications may be submitted for a branded product based on a product's regulatory exclusivity status, if no patents are listed in the Orange Book before the date on which a complete ANDA application for a product (excluding an amendment or supplement to the application) is submitted, an ANDA application could be approved by FDA without regard to a stay. For products entitled to five-year exclusivity status, the Hatch-Waxman Amendments provide that an ANDA application may be submitted after four years following FDA approval of the branded product if it contains a certification of patent invalidity or non-infringement to a patent listed in the Orange Book. In such a case, the 30-month stay runs from the end of the five-year exclusivity period. Statutory stays may be shortened or lengthened if either party fails to cooperate in the litigation and it may be terminated if the court decides the case in less than 30 months. If the litigation is resolved in favor of the ANDA applicant before the expiration of the 30-month period, the stay will be immediately lifted and the FDA's review of the application may be completed. Such litigation is often time-consuming and costly, and may result in generic competition if such patents are not upheld or if the generic competitor is found not to infringe such patents.

In the first half of 2014, we received six paragraph IV notices notifying us of accepted ANDAs to the Vascepa 1-gram dose strength under the Hatch-Waxman Amendments. These ANDAs were submitted and accepted by FDA under the

regulatory scheme adopted under the Hatch-Waxman Amendments based on the FDA's determination that we were entitled to three, and not five-year exclusivity. As a result, from the first half of 2014 until June 2015, we were engaged in costly litigation with the ANDA applicants to protect our patent rights.

Based on the May 28, 2015, District of Columbia court order granting our motion for summary judgment in the new chemical entity, or NCE, litigation, on June 26, 2015, the parties to the related Vascepa patent litigation that followed acceptance by FDA of ANDAs to Vascepa based on a three-year regulatory exclusivity determination, agreed to a full stay of proceeding in that patent litigation.

Following the May 28, 2015 District of Columbia court order setting aside FDA's denial of NCE exclusivity for Vascepa, FDA notified the ANDA filers that FDA had changed the status of their ANDAs to submitted, but no longer accepted, and notified ANDA filers that FDA had ceased review of the pending ANDAs. In rescinding acceptance of the ANDAs, the statutory basis for the patent litigation (accepted ANDAs) no longer existed. Thus, in July 2015, we moved to dismiss the pending patent infringement lawsuits against each of the Vascepa ANDA applicants in the U.S. District Court for the District of New Jersey.

On January 22, 2016, the U.S. District Court for the District of New Jersey granted our motion to dismiss all patent infringement litigation related to the 2014 acceptance by the FDA of ANDAs to Vascepa. An appeal of the court's dismissal was filed by one ANDA filer and, after FDA's May 2016 grant of Vascepa NCE exclusivity, that appeal was withdrawn by the ANDA filer. This dismissal and terminated appeal ended this patent litigation related to Vascepa.

On May 31, 2016, in a reversal that FDA and we view as consistent with the court's May 28, 2015 summary judgment motion, FDA determined that Vascepa is eligible for five-year, NCE marketing exclusivity. This determination provides Vascepa with the benefits of NCE exclusivity afforded by statute. NCE exclusivity for Vascepa ran from its date of FDA approval on July 26, 2012 and extended until July 26, 2017. We believe the statutory NCE-related 30-month stay triggered by the 1-gram dose patent litigation following generic application submissions permitted on July 26, 2016 is scheduled to continue until January 26, 2020, seven-and-a-half years from FDA approval, unless such patent litigation is resolved against us sooner.

In September and October 2016, we received paragraph IV certification notices from four companies contending to varying degrees that certain of our patents are invalid, unenforceable and/or will not be infringed by the manufacture, use, sale or offer for sale of a generic form of the 1-gram dose strength of Vascepa as described in those companies' ANDAs. These certifications were expected given the eligibility for submission of ANDAs under the NCE regulatory structure, after the expiration of four years from the July 2012 approval of Vascepa.

We filed patent infringement lawsuits against three of these four ANDA applicants. In October 2016, Amarin filed a lawsuit against Roxane Laboratories, Inc. and related parties, collectively, Roxane, in the U.S. District Court for the District of Nevada. The case against Roxane is captioned Amarin Pharma, Inc. et al. v. Roxane Laboratories, Inc. et al., Civ. A. No. 2:16-cv-02525 (D. Nev.). According to a stipulation filed with the Nevada court, in December 2016, Roxane transferred its ANDA to West-Ward Pharmaceuticals International Limited, which then designated West-Ward Pharmaceuticals Corp. (or together with West-Ward Pharmaceuticals International Limited, West-Ward) as its agent for FDA communications. In view of the ANDA transfer, in February 2017, West-Ward replaced Roxane and related parties as Defendants in the above-referenced case. The case against West-Ward is now captioned Amarin Pharma, Inc. et al. v. West-Ward Pharmaceuticals Corp. et al., Civ. A. No. 2:16-cv-02525 (D. Nev.). In November 2016, Amarin filed a lawsuit against Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd., collectively, DRL, in the U.S. District Court for the District of Nevada. The case against DRL is captioned Amarin Pharma, Inc. et al. v. Dr. Reddy's Laboratories, Inc. et al., Civ. A. No. 2:16-cv-02562 (D. Nev.). In November 2016, Amarin filed a lawsuit against Teva Pharmaceuticals USA, Inc. and Teva Pharmaceuticals Industries Limited, or collectively, Teva, in the U.S. District Court for the District of Nevada. The case against Teva was captioned Amarin Pharma, Inc. et al. v. Teva Pharmaceuticals USA, Inc. et al., Civ. A. No. 2:16-cv-02658. In all three lawsuits, we are seeking, among other remedies, an order enjoining each defendant from marketing generic versions of the 1-gram dose strength of Vascepa before the last to expire of the asserted patents in 2030. The three lawsuits have been consolidated for pretrial proceedings.

The fourth ANDA applicant referenced above is Apotex Inc., or Apotex, which sent us a paragraph IV certification notice in September 2016. The notice reflected that Apotex made a paragraph IV notice as to some, but not all, of the patents listed in the Orange Book for Vascepa. Because Apotex did not make a paragraph IV certification as to all listed patents, Apotex cannot market a generic version of Vascepa before the last to expire of the patents for which Apotex did not make a paragraph IV certification, which is in 2030. At a later date, Apotex may elect to amend its ANDA in order to make a paragraph IV certification as to additional listed patents. If and when Apotex does make such an amendment, it would be required to send Amarin an additional paragraph IV certification notice, and Amarin would then have the ability to file a lawsuit against Apotex pursuant to the Hatch-Waxman Amendments.

In October 2016, we introduced to the market a 0.5-gram dose strength of Vascepa. In August 2017, as anticipated, we received a paragraph IV certification notice from Teva contending that certain of our patents are invalid,

unenforceable and/or will not be infringed by the manufacture, use, sale or offer for sale of a generic form of the 0.5-gram dose strength of Vascepa, as described in the Teva ANDA. This Teva ANDA was filed as an amendment to the 1-gram Teva ANDA and is related to patents already at issue in the 1-gram Vascepa patent litigation. This certification followed the related listing in the Orange Book of patents associated with the 0.5-gram product in June 2017. This June 2017 listing was within the five-year, post NDA-approval period during which the Hatch-Waxman Amendments require a paragraph IV certification of patent invalidity or non-infringement under the Hatch-Waxman, five-year, NCE regulatory scheme. Accordingly, in October 2017, we filed a patent infringement lawsuit against Teva in the U.S. District Court for the District of Nevada. The case is captioned Amarin Pharma, Inc. et al. v. Teva Pharmaceuticals USA, Inc. et al., Civ. A. No. 2:17-cv-2641 (D. Nev.). In this lawsuit, we sought, among other remedies, an order enjoining Teva from marketing generic versions of the 0.5-gram dose strength of Vascepa before the last to expire of the asserted patents in 2030.

On May 24, 2018, we entered into a settlement agreement with Teva that resolves our ANDA patent litigation as it relates to Teva's as amended ANDA for both the 1-gram and 0.5-gram dose strengths of Vascepa. As part of this settlement agreement, Teva may first begin selling its generic version of Vascepa in the United States on August 9, 2029, or earlier under certain customary circumstances, including commercial launch by another generic manufacturer under certain circumstances, in which event Teva would

pay us certain royalties on its generic Vascepa products. The ANDA patent litigation continues in the United States District Court for the District of Nevada with parties West-Ward and DRL.

In July 2018, as anticipated, we received a paragraph IV certification notice from DRL contending that certain of our patents are invalid, unenforceable and/or will not be infringed by the manufacture, use, sale or offer for sale of a generic form of the 0.5-gram dose strength of Vascepa, as described in the DRL ANDA. This DRL ANDA was filed as an amendment to the 1-gram DRL ANDA and is related to patents already at issue in the 1-gram Vascepa patent litigation. This certification followed the related listing in the Orange Book of patents associated with the 0.5-gram product in June 2017. This June 2017 listing was within the five-year, post NDA-approval period during which the Hatch-Waxman Amendments require a paragraph IV certification of patent invalidity or non-infringement under the Hatch-Waxman, five-year, NCE regulatory scheme. Accordingly, in August 2018, we filed a patent infringement lawsuit against DRL in the U.S. District Court for the District of Nevada. The case is captioned Amarin Pharma, Inc. et al. v. Dr. Reddy's Laboratories, Inc. et al., Civ. A. No. 2:18-cv-01596 (D. Nev.). In this lawsuit, we are seeking, among other remedies, an order enjoining DRL from marketing generic versions of the 0.5-gram dose strength of Vascepa before the last to expire of the asserted patents in 2030. In light of the overlap between the cases, DRL and Amarin have stipulated that the final judgment on the merits of the parties' contentions in the consolidated 1-gram action shall also be binding in the 0.5-gram case.

We may also face challenges to the validity of our patents through a procedure known as inter partes review. Inter partes review is a trial proceeding conducted through the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office. Such a proceeding could be introduced against us within the statutory one-year window triggered by service of a complaint for infringement or at any time by an entity not served with a complaint. Such proceedings may review the patentability of one or more claims in a patent on specified substantive grounds such as allegations that a claim is obvious on the basis of certain prior art.

We intend to vigorously enforce our intellectual property rights relating to Vascepa, but we cannot predict the outcome of the pending lawsuits or any subsequently filed lawsuits or inter partes review.

If an ANDA filer meets the approval requirements for a generic version of Vascepa to the satisfaction of the FDA under its ANDA, FDA may grant tentative approval to the ANDA during a Hatch-Waxman 30-month stay period. A tentative approval is issued to an ANDA applicant when its application is approvable prior to the expiration of any exclusivities applicable to the branded, reference listed drug product. A tentative approval does not allow the applicant to market the generic drug product and postpones the final ANDA approval until any exclusivity protections, such as a 30-month stay, have expired. As a result of the statutory stays associated with the filing of these lawsuits under the Hatch-Waxman Amendments, we believe the FDA cannot grant final approval to West-Ward, DRL, or Teva's respective ANDAs for the 1-gram strength of Vascepa before January 26, 2020, unless there is an earlier court decision holding that the subject patents are not infringed and/or are invalid.

If final approval is granted and an ANDA filer is able to supply the product in significant commercial quantities, the generic company could introduce a generic version of Vascepa. Any such introduction of a generic version of Vascepa would also be subject to current patent infringement claims including those being litigated in the above-detailed patent litigations, and any court order we may seek and be granted to prevent any such launch based on our patent claims prior to any adverse court judgment or PTAB finding against us.

Any generic market entry would limit our U.S. sales, which would have a significant 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 our stock price.

Vascepa's five-year, NCE and related exclusivity benefits could be challenged by companies seeking to introduce generic versions of Vascepa.

The timelines and conditions under the ANDA process that permit the start of patent litigation and allow the FDA to approve generic versions of brand name drugs like Vascepa differ based on whether a drug receives three-year, or five-year, NCE marketing exclusivity. In May 2016, after significant litigation, FDA determined that Vascepa is eligible for NCE marketing exclusivity. Accordingly, we believe a related 30-month stay is currently in place with respect to our 1-gram dose strength of Vascepa that is scheduled to continue until January 26, 2020, seven-and-a-half years from FDA approval of Vascepa, unless related patent litigation is resolved against us sooner.

The FDA typically makes a determination on marketing exclusivity in connection with an NDA approval of a drug for a new indication. FDA marketing exclusivity is separate from, and in addition to, patent protection, trade secrets and manufacturing barriers to entry which could also help protect Vascepa against generic competition.

We applied to the FDA for five-year, NCE marketing exclusivity for Vascepa in connection with the NDA for our MARINE indication, which NDA was approved by the FDA on July 26, 2012. On February 21, 2014, in connection with the July 26, 2012

approval of the MARINE indication, the FDA denied a grant of five-year NCE marketing exclusivity to Vascepa and granted three-year marketing exclusivity. Under applicable regulations, such three-year exclusivity would have extended through July 25, 2015 and would have been supplemented by a 30-month stay triggered by patent litigation that would have extended into September 2016, unless such patent litigation was resolved against us sooner.

NCE marketing exclusivity precludes approval during the five-year exclusivity period of certain 505(b)(2) applications and ANDAs 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 such case, the pioneer drug company is afforded the benefit of a 30-month stay against the launch of such a competitive product that extends from the end of the five-year exclusivity period. A pioneer company could also be afforded extensions to the stay under applicable regulations, including a six-month pediatric exclusivity extension or a judicial extension if applicable requirements are met. A drug sponsor could also gain a form of marketing exclusivity under the Hatch-Waxman Amendments if such company can, under certain circumstances, complete a human clinical trial process and obtain regulatory approval of its product.

In contrast, a three-year period of exclusivity under the Hatch-Waxman Amendments is generally granted for a drug product that contains an active moiety that has been previously approved, such as 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. Accordingly, we expect to receive three-year exclusivity in connection with any future regulatory approvals of Vascepa, such as an approval sought based on positive REDUCE-IT outcomes study results. Such three-year exclusivity protection precludes the FDA from approving a marketing application for an ANDA, 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. The FDA may accept and commence review of such applications during the three-year exclusivity period. Such three-year exclusivity grant does not prevent a company from challenging the validity of patents at any time, subject to any prior four-year period pending from a grant of five-year exclusivity. 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.

On February 27, 2014, we sued the FDA in the U.S. District Court for the District of Columbia to challenge the agency's denial of five-year NCE exclusivity for Vascepa, based on our reading of the relevant statute, our view of FDA's inconsistency with its past actions in this area and the retroactive effect of what we believe is a new policy at FDA as it relates to our situation. On May 28, 2015, the court granted our motion for summary judgment. The decision vacated the FDA's denial of our claim for such exclusivity and remanded to the FDA for proceedings consistent with the decision. On July 22, 2015, Watson Laboratories Inc., the purported first Vascepa ANDA filer, sought to intervene and appeal the court's decision. We and FDA opposed this intervention effort. The applicable courts denied Watson the relief sought and appeal periods have expired.

On May 31, 2016, in a reversal that FDA and we view as consistent with the court's May 28, 2015 summary judgment motion, FDA determined that Vascepa is eligible for five-year, NCE marketing exclusivity. We believe this determination provides Vascepa with the benefits of NCE exclusivity afforded by statute. NCE exclusivity for Vascepa ran from its date of FDA approval on July 26, 2012 and extended until July 26, 2017. We believe the statutory NCE-related 30-month stay triggered by the 1-gram dose patent litigation following generic application submissions permitted on July 26, 2016 is scheduled to continue until January 26, 2020, seven-and-a-half years from FDA approval, unless such patent litigation is resolved against us sooner.

It is possible that FDA's NCE determination and related 30-month stay could be challenged by interested parties. If challenged, we plan to vigorously defend exclusivity for Vascepa. Any such challenge could have a negative impact on our company and create uncertainty around the continued benefits associated with exclusivity that we believe are

applicable to us under the Hatch-Waxman Amendments.

Regulatory exclusivity is in addition to exclusivity afforded by issued patents related to Vascepa.

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

Our only product, Vascepa, is a prescription-only form of EPA, an omega-3 fatty acid in ethyl ester form. Mixtures of omega-3 fatty acids in triglyceride form are naturally occurring substances contained in various foods, including fatty fish. Omega-3 fatty acids are marketed by others in a number of chemical forms as non-prescription dietary supplements. We cannot be sure physicians will view the pharmaceutical grade purity and proven efficacy and safety of Vascepa as having a superior therapeutic profile to unproven and loosely regulated omega-3 fatty acid dietary supplements. In addition, the FDA has not yet enforced to the full extent of its regulatory authority what we view as illegal claims made by certain omega-3 fatty acid product manufacturers to the extent we believe appropriate under applicable law and regulations, for example, claims that certain of such chemically altered products are dietary supplements and that certain of such products reduce triglyceride levels or could reduce cardiovascular risk.

Also, for more than a decade now, subject to certain limitations, the FDA has expressly permitted dietary supplement manufacturers that sell supplements containing the omega-3 fatty acids EPA and/or DHA to make the following qualified health claim directly to consumers: Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease. As a result of our First Amendment litigation and settlement, we may now make this claim to healthcare professionals subject to certain qualifications.

These factors enable dietary supplements to compete with Vascepa to a certain degree. Although we have taken steps to address these competitive issues, and plan to continue to do so vigorously, we may not be successful in such efforts. For example, on August 30, 2017, Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited, each wholly-owned subsidiaries of Amarin Corporation plc, filed a lawsuit with the United States International Trade Commission, or the ITC, against manufacturers, importers, and distributors of products containing synthetically produced omega-3 products in ethyl ester or re-esterified triglyceride form that contain more EPA than DHA or any other single component for use in or as dietary supplements. The lawsuit sought an investigation by the ITC regarding potentially unfair methods of competition and unfair acts involving the importation and sale of articles in the United States that injure or threaten injury to a domestic industry. On October 27, 2017, the ITC determined to not institute our requested investigation. We are currently appealing this determination in federal court and plan to pursue it vigorously. We have also recently sued several omega-3 dietary supplement manufacturers for making claims that we believe make them unfairly competitive to Vascepa.

In addition, to the extent the net price of Vascepa after insurance and offered discounts 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 and pharmacists may recommend these commercial alternatives instead of writing or filling prescriptions for Vascepa or patients may elect on their own to take commercially available omega-3 fatty acids. Also, insurance plans may increasingly impose policies that favor supplement use over Vascepa. While Vascepa is highly price-competitive for patients generally, and in particular when covered by insurance—cheaper in many cases—any 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.

We may not be successful in replacing our Vascepa co-promotion effort with Kowa Pharmaceuticals America, Inc. after it expired at the end of 2018.

In March 2014, we entered into a co-promotion agreement with Kowa Pharmaceuticals America, Inc. to co-promote Vascepa in the United States under which Kowa Pharmaceuticals America, Inc. co-promoted Vascepa in conjunction with its promotion of its primary product, a branded statin for patients with high cholesterol. Co-promotion under the agreement commenced in May 2014 and ceased at the end of 2018. We may seek to search for another commercialization partner, though there is no guarantee we would be successful in doing so. If we do not enter into a co-promotion agreement with an equally capable company or if our newly hired sales representatives are not effective as planned, our sales may be negatively impacted. If we elect to increase our expenditures to fund development or commercialization activities on our own, depending on Vascepa's revenues, we may 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. If we do not generate sufficient funds from the sale of Vascepa or, to the extent needed to supplement funds generated from product revenue, cannot raise sufficient funds, we may not be able to devote resources sufficient to market and sell Vascepa on our own in a manner required to realize the full market potential of Vascepa.

The commercial value to us of current and sought marketing rights 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 marketing rights we currently have or, if approved, an indication based on a successful outcome of the REDUCE-IT study. 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, the number of actual patients with conditions within the scope of our marketing efforts may be smaller than we anticipate. If any such marketing right or approved indication is narrower than we anticipate, the market potential for our product would suffer.

Our special protocol assessment, or SPA, agreement for ANCHOR was rescinded and our SPA agreement for REDUCE-IT is not a guarantee of FDA approval of Vascepa for proposed REDUCE-IT indications.

The REDUCE-IT trial was conducted pursuant to a SPA agreement, with the FDA, which means that the FDA agreed, based on the information we submitted to the agency, that the design and planned analysis of the trial was adequate to support use of the conducted study as the primary basis for approval with respect to effectiveness. A SPA agreement does not cover every aspect of clinical trial conduct and assessment. For example, secondary and/or tertiary endpoints, their ordering in the statistical hierarchy, their clinical significance, or whether any would yield results appropriate for labeling are considered review issues and are not intended to be a binding component of the REDUCE-IT SPA agreement. Further, matters such as endpoint adjudication procedures (including potential endpoint ascertainment, adjudication process and detailed definitions) were specified by FDA as issues to be reviewed by the

agency as part of a drug approval application. Consistent with the May 2016 FDA SPA draft guidance, FDA stated that the SPA agreement does not necessarily indicate the agency's agreement with every detail of a protocol; instead, such an agreement indicates FDA's concurrence with the elements critical to ensuring that the trial conducted under the protocol would have the potential to form the primary basis of an efficacy claim in a marketing application.

A SPA agreement is not a guarantee of approval. A SPA agreement 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. The FDA reserves the right of final determinations for approval based on its review of the entire data presented in a marketing application. The FDA previously rescinded our SPA agreement with the FDA for our ANCHOR trial because the FDA determined that a substantial scientific issue essential to determining the effectiveness of Vascepa in the studied population was identified after testing began. There can be no assurance that the FDA or the applicable regulatory authorities in other jurisdictions will not reach a similar conclusion with respect to the results of the REDUCE-IT trial or will not require additional studies by of Vascepa in additional patient populations.

The commercial value to us of sales of Vascepa outside the United States may be smaller than we anticipate.

There can be no assurance as to the adequacy for commercial success of Vascepa outside the United States. For example, even if we and Eddingpharm (Asia) Macao Commercial Offshore Limited, or Eddingpharm, obtain marketing approval in Mainland China, Hong Kong, Macau and Taiwan, or the China Territory, applicable regulatory agencies 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, there is a degree of unpredictability with regard to the eventual pricing and reimbursement levels of medications in markets outside the United States. If the pricing and reimbursement levels of Vascepa are lower than we anticipate, then affordability of, and market access to, Vascepa may be adversely affected and thus market potential in these territories would suffer. Furthermore, with regard to any indications for which we may gain approval in territories outside the United States, 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 in these countries for our product would suffer.

Our products and marketing efforts are 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-healthcare provider and 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. The result of our First Amendment litigation and settlement may cause the government to scrutinize our promotional efforts or otherwise monitor our business more closely. 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 pharmaceutical 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 federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, enacted in March 2010, which require manufacturers of certain drugs, devices, 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. We must also comply with requirements to collect and report adverse events and product complaints associated with our products. For example, in September 2014, we participated in a routine inspection from the FDA in which the FDA made observations on perceived deficiencies related to our processes for collection and processing of adverse events. We have responded to FDA with respect to these observations and continue to work with FDA to show that we have improved related systems and, given we received communication from the FDA that it considers this matter to be closed, we believe that we have demonstrated to FDA that we have adequately responded to these observations. Our activities are also subject to U.S. federal and state consumer protection and unfair competition laws, non-compliance with which could subject us to significant liability. 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. We may also be held responsible for the non-compliance of our partners, such as Kowa Pharmaceuticals America, Inc. In addition, even if we 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. Newly discovered or developed safety or effectiveness data may require changes to a drug's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Adverse regulatory action, whether pre- or post-approval, can potentially lead to product liability claims and increase our product liability exposure. We must also compete against other products in qualifying for coverage and reimbursement under applicable third-party payment and insurance programs. In addition, all of the above factors may also apply to any regulatory approval for Vascepa obtained in territories outside the United States. Given our inexperience with marketing and commercializing products outside the United States, we will need to rely on third parties, such as Eddingpharm in China, to assist us in dealing with any such issues.

Legislative or regulatory reform of the healthcare 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 healthcare services to contain or reduce healthcare 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 healthcare system in ways that could affect our ability to sell our products profitably. For example, beginning April 1, 2013, Medicare payments for all items and services, including drugs and biologics, were reduced by 2% under the sequestration (i.e., automatic spending reductions) required by the Budget Control Act of 2011, as amended by the American Taxpayer Relief Act of 2012. Subsequent legislation extended the 2% reduction, on average, to 2027. These cuts reduce reimbursement payments related to our products, which could potentially negatively impact our revenue. Also for example, the ACA substantially changed the way healthcare is financed by both governmental and private insurers. Among other cost-containment measures, ACA 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;
- a new formula that increases the rebates a manufacturer must pay under the Medicaid Drug Rebate Program; and
- new policies or laws affecting Vascepa sales, such as state and federal efforts to affect drug pricing and provide healthcare coverage that includes reimbursement for prescription drugs.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under

Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a “Blueprint” to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated

that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, the State of California enacted legislation that requires notice for exceeding specified limits on annual drug price increases and other legislation that seeks to limit the use of co-pay cards in certain situations.

In addition, it is 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 ACA and by other healthcare 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. For example, proposals are being considered to expand the use of dietary supplements in addition to or in place of drugs in government and private payor plans. In addition, 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.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We participate in the Medicaid Drug Rebate program, the 340B drug pricing program, and the U.S. Department of Veterans Affairs, or VA, Federal Supply Schedule, or FSS, pricing program. Under the Medicaid Drug Rebate program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by us on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Our failure to comply with these price reporting and rebate payment obligations could negatively impact our financial results.

The ACA made significant changes to the Medicaid Drug Rebate program. CMS issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate program under the ACA. The issuance of the final regulation has increased and will continue to increase our costs and the complexity of compliance, has been and will continue to be time-consuming to implement, and could have a material adverse effect on our results of operations, particularly if CMS challenges the approach we take in our implementation of the final

regulation.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service's 340B drug pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and Medicaid rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the ACA, other legislation, or in regulation could affect our 340B ceiling price calculations and negatively impact our results of operations.

The Health Resources and Services Administration, or HRSA, which administers the 340B program, issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, which became effective on January 1, 2019. It is currently unclear how HRSA will apply its enforcement authority under the new regulation. HRSA also is implementing a ceiling price reporting requirement related to the 340B

program during the first quarter of 2019, pursuant to which we are required to report our 340B ceiling prices to HRSA on a quarterly basis. Implementation of the civil monetary penalties regulation and the issuance of any other final regulations and guidance could affect our obligations under the 340B program in ways we cannot anticipate. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in the inpatient setting.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. In the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we are required to offer our products under the 340B program or could require us to issue refunds to 340B covered entities.

Significant civil monetary penalties can be applied if we are found to have knowingly submitted any false pricing information to CMS, or if we fail to submit the required price data on a timely basis. Such conduct also could be grounds for CMS to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. Significant civil monetary penalties also can be applied if we are found to have knowingly and intentionally charged 340B covered entities more than the statutorily mandated ceiling price. We cannot assure you that our submissions will not be found by CMS or HRSA to be incomplete or incorrect.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, we participate in the U.S. Department of Veterans Affairs, or VA, Federal Supply Schedule, or FSS, pricing program. As part of this program, we are obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory Federal Ceiling Price, or FCP, to four federal agencies (VA, U.S. Department of Defense, or DOD, Public Health Service, and U.S. Coast Guard). The FCP is based on the Non-Federal Average Manufacturer Price, or Non-FAMP, which we calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant penalties for each item of false information. These obligations also contain extensive disclosure and certification requirements.

We also participate in the Tricare Retail Pharmacy program, under which we pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP. We are required to list our covered products on a Tricare Agreement in order for these products to be eligible for DOD formulary inclusion. If we overcharge the government in connection with our FSS contract or Tricare Agreement, whether due to a misstated FCP or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Changes in reimbursement procedures by government and other third-party payors may limit our ability to market and sell our approved drugs. These changes could have a material adverse effect on our business and financial condition.

In the U.S. and abroad, sales of pharmaceutical drugs are dependent, in part, on the availability of reimbursement to the consumer from third-party payors, such as government and private insurance plans. Third-party payors are increasingly challenging the prices charged for medical products and services. Some third-party payor benefit packages restrict reimbursement, charge copayments to patients, or do not provide coverage for specific drugs or drug classes.

In addition, certain healthcare providers are moving toward a managed care system in which such providers contract to provide comprehensive healthcare services, including prescription drugs, for a fixed cost per person. We are unable to predict the reimbursement policies employed by third-party healthcare payors.

We expect to experience pricing and reimbursement pressures in connection with the sale of our products due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals. In addition, we may confront limitations in insurance coverage for our products. If we fail to successfully secure and maintain reimbursement coverage for our approved drugs or are significantly delayed in doing so, we may have difficulty achieving market acceptance of our approved drugs and investigational drug candidates for which we obtain approval, and our business may be harmed. Congress has enacted healthcare reform and may enact further reform, which could adversely affect the pharmaceutical industry as a whole, and therefore could have a material adverse effect on our business.

Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.

Some of the provisions of the ACA have yet to be fully implemented, and certain provisions have been subject to judicial and Congressional challenges. In addition, there have been efforts by the Trump administration to repeal or replace certain aspects of the ACA and to alter the implementation of the ACA and related laws. Since January 2017, the Trump administration has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Nineteen state Attorneys General filed suit to stop the administration from terminating the subsidies, but on July 18, 2018, the U.S. District Court for the Northern District of California dismissed the case without prejudice. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that, due to Congressional appropriations riders that prohibited the Department of Health and Human Services (HHS) from paying out more in risk corridor payments than it collected, HHS was not required to pay more than \$12 billion in ACA risk corridor payments owed to insurers under the risk corridor formula. On November 6, 2018, the Federal Circuit declined to rehear the case en banc. Insurers have appealed this ruling to the Supreme Court.

Moreover, the Tax Cuts and Jobs Act enacted on December 22, 2017, eliminated the tax-based shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code of 1986, commonly referred to as the “individual mandate,” effective January 1, 2019. On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to reduce the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole” by raising the manufacturer discount under the Medicare Part D coverage gap discount program to 70%.

In July 2018, the Centers for Medicare and Medicaid Services, or CMS, published a final rule permitting certain further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. In addition, CMS has published a final rule that gives states greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseparable feature of the ACA, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act of 2017, the remaining provisions of the ACA are invalid

as well. This ruling is under appeal and stayed pending appeal. While the Trump Administration and CMS have both stated that the ruling will have no effect while this appeal is pending, it is unclear how this decision, subsequent appeals, and other efforts to invalidate the ACA or portions thereof will impact the ACA, its implementation, and our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. In August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction, which triggered the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of, on average, 2% per fiscal year through 2025 unless Congress takes additional action. These reductions were extended through 2027 under the BBA. In January 2013, the American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria, and new payment methodologies, and in additional downward pressure on coverage and payment and the

price that we receive for any approved product, and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private third-party payors.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and any potential collaborators may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA – other than with respect to providing certain employee benefits – we could potentially be subject to criminal penalties if we, our affiliates, or our agents knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

European data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.

In the event we decide to conduct clinical trials in the European Union, or EU, we may be subject to additional privacy restrictions. The collection and use of personal health data in the EU is governed by the provisions of the General Data Protection Regulation, or GDPR. This directive imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the

United States. Failure to comply with the requirements of the Data Protection Directive, the GDPR, and the related national data protection laws of the European Union Member States may result in fines and other administrative penalties. The GDPR introduces new data protection requirements in the European Union and substantial fines for breaches of the data protection rules. The GDPR regulations may impose additional responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with these and/or new data protection rules. This may be onerous and adversely affect our business, financial condition, prospects and results of operations.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. If we or our partners are found to have improperly promoted uses, efficacy or safety of Vascepa, we may become subject to significant fines and other liability. The government may seek to find means to prevent our promotion of truthful and non-misleading information beyond the current court ruling and litigation settlement.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. In particular, in general, the U.S. government's position has been that a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. Even though we received FDA marketing approval for Vascepa for the MARINE indication and we believe the First Amendment court ruling and litigation settlement affords us a degree of protection for

other promotional efforts, physicians may still prescribe Vascepa to their patients for use in the treatment of conditions that are not included as part of the indication statement in our FDA-approved Vascepa label or our settlement. If we are found to have promoted Vascepa outside the terms of the litigation settlement or in violation of what federal or state government may determine to be acceptable, we may become subject to significant government fines and other related liability, such as under the FDCA, the False Claims Act, or other theories of liability. Government may also seek to hold us responsible for the non-compliance of our former co-promotion partner, Kowa Pharmaceuticals America, Inc., or our commercialization partners outside the United States. 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 we 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.

Even though we have a final settlement in our litigation related to promotion beyond FDA-approved labeling, our promotion would still be subject to a high, perhaps abnormally high, degree of scrutiny to ensure that our promotion remains within the permitted scope. Likewise, federal or state government may seek to find other means to prevent our promotion of truthful and non-misleading information.

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 and elsewhere. In the United States, the FDA generally requires preclinical 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 but not limited to:

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

government or regulatory delays or “clinical holds” requiring suspension or termination of a trial; and political instability affecting our clinical trial sites.

Even if we obtain positive results from early stage preclinical studies 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. Questions can also arise on the quality of study data or its reliability. For example, during the public advisory committee meeting held by FDA as part of its review of our ANCHOR sNDA, a

discussion regarding observed, nominally statistically significant changes from baseline in an adverse direction, while on background statin therapy, in certain lipid parameters, including triglycerides, in the placebo group, raised questions about the possibility that the mineral oil placebo used in the ANCHOR trial (and in the REDUCE-IT trial) might not be biologically inert and might be viewed as artificially exaggerating the clinical effect of Vascepa when measured against placebo in the ANCHOR trial. Ultimately, no strong evidence for biological activity of mineral oil was identified by the FDA before its approval of Vascepa after review of the MARINE and ANCHOR trials and consideration of other data regarding mineral oil. It was ultimately concluded that the between-group differences likely provided the most appropriate descriptions of the treatment effect of Vascepa and that whatever factor(s) led to the within-group changes over time in the placebo group were likely randomly distributed to all treatment groups. Thus, the FDA approved Vascepa for use in the MARINE indication in July 2012, FDA did not dispute the veracity of the ANCHOR trial data and, in connection with the March 2016 agreement we reached with the FDA allowing us to promote the results of the ANCHOR study, the FDA did not seek to require that we include any qualification related to this earlier question regarding the mineral oil placebo. The FDA, early on in the course of the REDUCE-IT trial, directed the DMC for REDUCE-IT to periodically review unblinded lipid data to monitor for signals that the placebo might not be inert. After each such quarterly unblinded safety analysis and review meeting to date, the DMC recommended to continue the REDUCE-IT study as planned. Each of these DMC recommendations has been shared with FDA. This matter illustrates that concerns such as this may arise in the future that could affect our product development, regulatory review or the public perception of our products and our future prospects, including REDUCE-IT results.

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 gain approval for new indications and affect revenues from the sale of our 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 clinical trial or product, or in connection with the manufacturer of products, may result in regulatory issues that prevent proposed future approvals of a product and/or restrictions on that product or manufacturer, including withdrawal of an indication or the product from the market, which would have a negative impact on our potential revenue stream.

As we continue to 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.

The process of establishing a commercial infrastructure is difficult, expensive and time-consuming. Prior to REDUCE-IT topline results announcement in September 2018, our sales team consisted of approximately 170 sales professionals, including sales representatives and their managers. We have recently increased the size of our sales force approximately 440 sales professionals, including approximately 400 sales representatives, in the United States and are expanding our promotion of Vascepa. This sales team promotes Vascepa to a limited group of physicians and other healthcare professionals in select geographies in the United States. Even after planned expansion, this sales team is not large enough to call upon all physicians.

In addition to sales force expansion in the United States, Amarin plans to work with its international partners to support regulatory efforts outside the United States based on REDUCE-IT results. As our operations expand with the anticipated growth of our product sales, 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 the commercial market and clinical trials is dependent upon relationships with third-party manufacturers and suppliers.

We have no in-house manufacturing capacity and rely on contract manufacturers for our clinical and commercial product supply. We cannot ensure 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 our manufacturers 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.

Any manufacturing problem, natural disaster affecting manufacturing facilities, government action, or the loss of a contract manufacturer could be disruptive to our operations and result in lost sales. 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/or result in lost sales. If our suppliers were unable to supply us with adequate volumes of active pharmaceutical ingredient (drug substance) or encapsulated bulk product (drug product), it would have a material adverse effect on our ability to continue to commercialize Vascepa.

We have contractual freedom to source the API for Vascepa and to procure other services supporting our supply chain. We have entered into supply agreements with multiple suppliers who also rely on other third-party suppliers to manufacture the API and other elements necessary for the sale of Vascepa. Our strategy in sourcing API and other components in our supply chain from multiple suppliers has been to expand manufacturing capacity, maintain competitive advantages, and mitigate the risk of reliance on any single supplier.

Expanding manufacturing capacity and qualifying such capacity is complex and subject to numerous regulations and other operational challenges. The resources of our suppliers vary and are limited; costs associated with projected expansion and qualification can be significant. 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 continued qualification of our API suppliers and, depending on the ability of existing suppliers to meet our supply demands, potentially the qualifications of new suppliers. Each of our API suppliers has outlined plans for potential further capacity expansion. If no additional API supplier is approved by the FDA as part of an sNDA, our API supply will be limited to the API we purchase from previously approved suppliers. If our third-party manufacturing capacity is not expanded and/or compliant with applicable regulatory requirements, we may not be able to supply sufficient quantities of Vascepa to meet anticipated demand. We cannot guarantee 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.

There can be no guarantee that current suppliers and future suppliers with which we have contracted to encapsulate API will be continually qualified to manufacture the product to our specifications or that current and any future suppliers will have the manufacturing capacity to meet anticipated demand for Vascepa.

We may 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.

Certain of our agreements with our suppliers 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. Certain of our agreements also include contractual minimum purchase commitments regardless of the rolling twelve-month forecasts. 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, packaging and distribution of pharmaceutical products such as Vascepa are subject to FDA regulations 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, packaging and distribution 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 pharmaceutical current good manufacturing practices, or cGMPs, and comparable requirements of foreign regulatory bodies. There are a limited number of manufacturers that operate under these cGMPs and International Council for Harmonisation of

Technical Requirements for Registration of Pharmaceuticals for Human Use, or ICH, regulations and guidelines 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 voluntary recalls of product, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business. If we are not able to manufacture Vascepa to required specifications through our current and 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 pre-approval of the manufacturing process and procedures in accordance with the FDA's 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 under ICH guidelines. This review may be costly and time consuming and could delay or prevent the launch of a product.

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 demonstrated 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 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 requirements, or change their interpretation and enforcement of existing requirements, for manufacture, packaging or testing of products at any time. If we or our approved suppliers are unable to comply, we may be subject to regulatory, civil actions or penalties which could significantly and adversely affect our business.

Our commercialization of Vascepa outside the United States is substantially dependent on third parties.

We have expanded our Vascepa commercialization activities outside of the United States through several contractual arrangements in territories including China, the Middle East, North Africa and Canada. We continue to assess other opportunities to develop Vascepa commercialization outside of the United States through similar arrangements.

In February 2015, we entered into a Development, Commercialization and Supply Agreement, or the DCS Agreement, with Eddingpharm related to the development and commercialization of Vascepa in the China Territory. Under the DCS Agreement, Eddingpharm is responsible for development and commercialization activities in the China Territory and associated expenses. Additionally, Eddingpharm is required to conduct clinical trials in the China Territory to secure regulatory approval in certain territories. For example, in December 2017, Eddingpharm commenced a pivotal clinical trial aimed to support the regulatory approval of the first indication of Vascepa in a patient population with severe hypertriglyceridemia in Mainland China. Additional clinical development efforts may be necessary in this market. Significant commercialization of Vascepa in the China Territory is several years away, if at all. If Eddingpharm is not able to effectively develop and commercialize Vascepa in the China Territory, we may not be able to generate revenue from the DCS Agreement resulting from the sale of Vascepa in the China Territory.

In March 2016, we entered into an agreement with Biologix FZCo, or Biologix, to register and commercialize Vascepa in several Middle Eastern and North African countries. Under the terms of the distribution agreement, we granted to Biologix a non-exclusive license to use our trademarks in connection with the importation, distribution, promotion, marketing and sale of Vascepa in the Middle East and North Africa territory. Commercialization across the Middle East and North Africa is several years away, if at all, in the most commercially significant territories and subject to similar risks as in the China Territory.

In September 2017, we entered into an agreement with HLS Therapeutics Inc., or HLS, to register, commercialize and distribute Vascepa in Canada. Under the agreement, HLS is responsible for regulatory and commercialization activities and associated costs. Amarin is responsible for providing assistance towards local filings, supplying finished product under negotiated supply terms, maintaining intellectual property, and continuing the development and funding of REDUCE-IT-related activities. Significant commercialization of Vascepa in Canada is several years away, if at all. If HLS Therapeutics is not able to effectively register and commercialize Vascepa in Canada, we may not be able to generate revenue from the agreement as a result of the sale of Vascepa in Canada.

We have limited experience working with partners outside the United States to develop and market our products in non-U.S. jurisdictions. In order for our partners to market and sell Vascepa in any country outside of the United States for any indication, it will be necessary to obtain regulatory approval from the appropriate regulatory authorities. The requirements and timing for regulatory approval, which may include conducting clinical trials, vary widely from

country to country and may in some cases be different than or more rigorous than requirements in the United States. Any failure by us or our partners to obtain approval for Vascepa in non-U.S. jurisdictions in a timely manner may limit the commercial success of Vascepa and our ability to grow our revenues.

Our dependence on third parties in the distribution channel from our manufacturers to patients subject us to risk that limit our profitability and could limit our ability to supply Vascepa to large market segments.

We sell Vascepa principally to a limited number of major wholesalers, as well as selected regional wholesalers and specialty pharmacy providers, or collectively, our Distributors or our customers, that in turn resell Vascepa to retail pharmacies for subsequent resale to patients and healthcare providers. These parties exercise a substantial amount of bargaining power over us given their control over large segments of the market for Vascepa. This bargaining power has led us to bear increasingly higher discounts in the sale of Vascepa. In addition, payors have broad latitude to change individual products' formulary position or to implement other barriers that inhibit patients from receiving therapies prescribed by their healthcare professionals. These payor barriers include requirements that patients try another drug before Vascepa, known as step edits, and the requirement that prior authorization be obtained by a healthcare provider after a prescription is written before a patient will be reimbursed by their health plan for the cost of a Vascepa prescription. Further, pharmacy benefit managers implement plans that act as disincentives for Vascepa use, such as increasingly higher

deductibles. One practical impact of higher deductibles is that they cause patients to delay filling prescriptions for asymptomatic, chronic care medications such as hypertriglyceridemia earlier in the year, until patients meet their deductible and the cost of Vascepa is then borne more by their insurance carrier. Collectively, these dynamics negatively affect our profitability for the sale of Vascepa and could increase over time further impacting our operating results. Consolidation among these industry participants could increase the pressure from these market dynamics.

Our relationships with healthcare providers and physicians and third-party payors are subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose use to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of pharmaceutical products. Arrangements with third-party payors and customers can expose pharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute pharmaceutical products. In particular, the promotion, sales and marketing of healthcare items and services, as well as a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. The applicable federal and state healthcare laws and regulations laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. Liability may be established without a person or entity having actual knowledge of the federal anti-kickback statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

Although there are a number of statutory exemptions and regulatory safe harbors protecting certain activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants or patient or product support programs;

- the federal Civil False Claims Act (FCA), which prohibits, among other things, any person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of government funds, or knowingly making or using, or causing to be made or used, a false record or statement material to an obligation to pay money to the government or knowingly concealing, or knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. The FCA also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the statute and to share in any monetary recovery. Recently, several pharmaceutical and other healthcare companies have been investigated or faced enforcement actions under the FCA for a variety of alleged improper marketing activities, including allegations that they caused false claims to be submitted because of the company’s marketing of the product for unapproved, and thus allegedly non-reimbursable, uses. Federal enforcement agencies also have showed increased interest in pharmaceutical companies’ product and patient assistance programs, including reimbursement and co-pay support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs;

•HIPAA, which, among other things, imposes criminal and civil liability for knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payor and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services;

•HIPAA, and its implementing regulations, which impose, among other things, requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;

50

the federal Physician Payment Sunshine Act, being implemented as the Open Payments Program, which requires manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to direct or indirect payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held in the company by physicians and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives;

federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and other state or local laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs; require drug manufacturers to report information related to clinical trials, or information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and/or require identification or licensing of sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies continue to give regular and close scrutiny to interactions between healthcare companies and healthcare providers, and such scrutiny often leads to investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business.

The failure to comply with any of these laws or regulatory requirements subjects entities to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in federal and state funded healthcare programs (such as Medicare and Medicaid), contractual damages and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Any action for violation of these laws, even if successfully defended, could cause a pharmaceutical manufacturer to incur significant legal expenses and divert management's attention from the operation of the business. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way.

Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us

from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

In addition, the approval and commercialization of any of our AXA Candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

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 trials. Moreover, the FDA requires us to comply with requirements, commonly referred to as good clinical practices, for conducting, recording, and reporting the results of clinical trials to ensure 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

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

Our success depends in part on our ability to obtain and maintain intellectual property protection for our drug candidates, technology and know-how, and to operate without infringing the proprietary rights of others. Our ability to successfully implement our business plan and to protect our products with our intellectual property 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.

We have prosecuted, and are currently prosecuting, multiple patent applications to protect the intellectual property developed during the Vascepa development program. As of the date of this report, we had 79 patent applications in the United States that have been either issued or allowed and more than 30 additional patent applications are pending in the United States. Such 79 allowed and issued applications include the following:

- 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;
- 43 U.S. patents covering or related to the use of Vascepa in either the MARINE or ANCHOR populations that have terms that expire in 2030 or later;
- 1 U.S. patents covering or related to the use of Vascepa in the REDUCE-IT population with terms expiring in 2033 or later;
- 4 additional patents related to the use of a pharmaceutical composition comprised of free fatty acids to treat the ANCHOR patient population with a term that expires in 2030 or later;
- 2 additional patents related to the use of a pharmaceutical composition comprised of free fatty acids to treat the MARINE patient population with a term that expires in 2030;
- 3 additional patents related to the use of a pharmaceutical composition comprised of free fatty acids to treat the REDUCE-IT population expiring 2033;
- 1 additional patent related to a pharmaceutical composition comprised of free fatty acids and uses thereof to treat both the MARINE and ANCHOR patient populations with a term that expires in 2030;
- 1 additional patent related to the use of a pharmaceutical composition comprised of re-esterified EPA triglyceride to treat the REDUCE-IT population expiring 2033;
- 3 additional patents related to a formulation of EPA/DHA and uses thereof with a term that expires in 2030;
- 2 additional patents related to the use of Vascepa to treat obesity with a term that expires in 2034;
- 2 additional patents covering a pharmaceutical composition comprised of EPA and a hydroxyl compound with a term that expires in 2034; and
- 4 additional patents covering a new combination therapy comprised of EPA and another drug.

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 applications with issued notices of allowance will be issued as patents or that

any of our pending patent applications will issue as patents. No assurance can be given that, if and when issued, our patents will prevent competitors from competing with Vascepa. For example, we may choose to not assert all issued patents in patent litigation and patents or claims within patents may be determined to be invalid.

We are the owner of the above-listed patents. We are also the exclusive licensee of certain patents owned by others covering products in development. To secure our debt under our outstanding royalty-like instrument, we have granted the holders of such instrument a security interest in our Vascepa-related patents.

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, including, for example, under our collaboration with Mochida. 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. For example, one of our patents was revoked in an opposition proceeding in Europe due to a determination of improper claim amendments under a provision of law not applicable in the United States. 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 may not prevent competitors from competing with Vascepa, even if we seek to enforce our patent rights.

We plan to vigorously defend our rights under issued patents. For example, in March 2014, we filed a patent infringement suit against Omthera Pharmaceuticals, Inc., and its parent company, AstraZeneca Pharmaceuticals LP. The suit sought injunctive relief and monetary damages for infringement of our U.S. Patent No. 8,663,662. The complaint alleged infringement of the patent arising from the expected launch of Epanova, a product that is expected to compete with Vascepa in the United States. The patent covers methods of lowering triglycerides by administering a pharmaceutical composition that includes amounts of EPA as free acid, and no more than about 30% DHA. In November 2014, based on a representation from AstraZeneca Pharmaceuticals LP that the commercial launch of Epanova was not imminent, the court dismissed our complaint, without prejudice (i.e., preserving our ability to later re-file the suit). The court required the defendant to notify us before any product launch. We intend to pursue this litigation vigorously and aggressively protect its intellectual property rights. However, patent litigation is a time-consuming and costly process. There can be no assurance that we will be successful in enforcing this patent or

that it will not be successfully challenged and invalidated. Even if we are successful in enforcing this patent, the process could take years to reach conclusion.

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.

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 these additional MARINE and ANCHOR patents or any of our pending patent applications intended to cover an indication based on results from the REDUCE-IT clinical trial will be granted or, if they grant, that they will prevent competitors from competing with Vascepa.

For example, we expect to engage in new ANDA patent litigation in the United States and elsewhere with respect to method of use patents related to the REDUCE-IT study after any newly granted indications based on that study.

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.

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.

In addition to our patent portfolio and strategy, 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

If the estimates we make, or the assumptions on which we rely, in preparing our projected guidance prove inaccurate, our actual results may vary from those reflected in our projections and accruals.

In January 2019, we issued financial and business guidance, including expected fiscal year 2019 total net revenue and expectations regarding inventory build, 2019 operating expenses, and timing of an sNDA seeking Vascepa label expansion. All such guidance is based on estimates and the judgment of management. Because of the inherent nature of estimates, there could be significant differences between our estimates and the actual amount of product demand. If, for any reason, we are unable to realize our currently projected 2019 revenue, we may not realize our publicly announced financial guidance. If we fail to realize or if we change or update any element of our publicly disclosed financial guidance as we have done in the past or other expectations about our business change, our stock price could decline in value.

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

We are engaged in the pharmaceutical 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 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.

Our internal computer systems, or those of our third party clinical research organizations or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our research and development programs.

Despite the implementation of security measures, our internal computer systems and those of our third party clinical research organizations and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. While we have not experienced any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or products candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and our research and development program could be delayed.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company and our vendors, including personal information of our employees and patients, and company and vendor confidential data. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our personnel or the personnel of our vendors to disclose sensitive information in order to gain access to our data and/or systems. We may experience threats to our data and systems, including malicious codes and viruses, phishing and other cyber-attacks. The number and complexity of these threats continue to increase over

time. If a material breach of our information technology systems or those of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. In addition, we could be subject to regulatory actions and/or claims made by individuals and groups in private litigation involving privacy issues related to data collection and use practices and other data privacy laws and regulations, including claims for misuse or inappropriate disclosure of data, as well as unfair or deceptive practices. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. As we outsource more of our information systems to vendors, engage in more electronic transactions with payors and patients, and rely more on cloud-based information systems, the related security risks will increase and we will need to expend additional resources to protect our technology and information systems. In addition, there can be no assurance that our internal information technology systems or those of our third-party contractors, or our consultants' efforts to implement adequate security and control measures, will be sufficient to protect us against breakdowns, service disruption, data deterioration or loss in the event of a system malfunction, or prevent data from being stolen or corrupted in the event of a cyberattack, security breach, industrial espionage attacks or insider threat attacks which could result in financial, legal, business or reputational harm.

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.

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 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. Our and our subsidiaries' income tax returns are periodically examined by various tax authorities, including the Internal Revenue Service (IRS) and states. We recently completed the audits by the IRS for the years 2013 to 2014, with no material changes to the filed income tax returns. Although the outcome of tax audits is always uncertain and could result in significant cash tax payments, we do not believe the outcome of any future audits

will have a material adverse effect on our consolidated financial position or results of operations. The ultimate resolution may result in a payment that is materially different from our current estimate of the tax liabilities. 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 effect on us of comprehensive U.S. tax reform legislation whether adverse or favorable, is uncertain.

On December 22, 2017, President Trump signed into law H.R. 1, “An Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018”, or informally, the Tax Cuts and Jobs Act. Among a number of significant changes to the U.S. federal income tax rules, the Tax Cuts and Jobs Act reduces the marginal U.S. corporate income tax rate from 35% to 21%, limits the deduction for net interest expense, shifts the United States toward a more territorial tax system, and imposes new taxes to combat erosion of the U.S. federal income tax base. The effect of the Tax Cuts and Jobs Act on our company and our affiliates, whether adverse or favorable, is uncertain, and may not become evident for some period of time. You are urged to consult your tax adviser regarding the implications of the Tax Cuts and Jobs Act for an investment in our ADSs.

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.

We could be adversely affected by our exposure to customer concentration risk.

A significant portion of our sales are to wholesalers in the pharmaceutical industry. Three customers individually accounted for 10% or more of our gross product sales. Customers A, B, and C accounted for 31%, 30%, and 27%, respectively, of gross product sales for the year ended December 31, 2018 and represented 26%, 24%, and 39%, respectively, of the gross accounts receivable balance as of December 31, 2018. Customers A, B, and C accounted for 27%, 33%, and 28%, respectively, of gross product sales for the year ended December 31, 2017 and represented 27%, 21%, and 41%, respectively, of the gross accounts receivable balance as of December 31, 2017. There can be no guarantee that we will be able to sustain our accounts receivable or gross sales levels from our key customers. If, for any reason, we were to lose, or experience a decrease in the amount of business with our largest customers, whether directly or through our distributor relationships, our financial condition and results of operations could be negatively affected.

Risks Related to Our Financial Position and Capital Requirements

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

We have not yet reached profitability. For the fiscal years ended December 31, 2018, 2017, and 2016, we reported losses of approximately \$116.4 million, \$67.9 million, and \$86.4 million, respectively, and we had an accumulated deficit as of December 31, 2018 of \$1.4 billion. 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 costs related to the commercialization of Vascepa. 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. 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.

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. We have been generating product revenue from sales of Vascepa since January 2013, 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 effectively market and sell Vascepa through our strategic collaborations.

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 in the near term due to high costs associated with our REDUCE-IT study and commercialization efforts, for example. If we are unable to continue to generate robust product revenues, we will not become profitable in the near term, if ever, 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 commercial launch of Vascepa in 2013 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 with ANCHOR data and seek to obtain additional regulatory approval of Vascepa from 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. Vascepa sales are 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 continuing evolution of the medical community's and the public's perception of the REDUCE-IT study results;
- the level of demand for Vascepa, due to changes in prescriber sentiment, quarterly changes in Distributor purchases, and other factors;
- 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 and the timing and extent to which such coverage and reimbursement changes;
- the timing, cost and level of investment in our sales and marketing efforts to support Vascepa sales and the resulting effectiveness of those efforts with our co-promotion partner, Kowa Pharmaceuticals America, Inc.;
- the timing and ability of commercialization partners outside the United States, to develop, register and commercialize Vascepa in the China Territory, several Middle Eastern and North African countries, and Canada, for example, including obtaining necessary regulatory approvals and establishing marketing channels;
- additional developments regarding our intellectual property portfolio and regulatory exclusivity protections, if any;
- outcomes of litigation and other legal proceedings; and
- our regulatory dialogue on the REDUCE-IT study.

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. We believe that our cash and cash equivalents balance of \$249.2 million as of December 31, 2018, will be sufficient to fund our projected operations for at least twelve months and through the likely Prescription Drug User Fee Act (PDUFA) date for approval of a supplemental new drug application (sNDA) by the FDA based on REDUCE-IT study results. Depending on the level of cash generated from operations, and depending in part on the timing and results of the FDA review of the sNDA and rate of prescription growth for Vascepa, additional capital may be required to support planned expansion of Vascepa promotion and potential Vascepa promotion beyond which we are currently executing. If additional capital is required and we are unable to obtain additional capital, we may be forced to delay, limit or eliminate certain promotional activities. We anticipate that quarterly net cash outflows in future periods will be variable.

In order to fully realize the market potential of Vascepa, we may need to enter into a new strategic collaboration or raise additional capital.

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

- the timing, amount and consistency of revenue generated from the commercial sale of Vascepa;
- the costs associated with commercializing Vascepa in the United States, including expenditures such as potential direct-to-consumer advertising and increased sales force sizing, and for additional indications in the United States and in jurisdictions in which we receive regulatory approval, if any, the cost and timing of securing commercial supply of Vascepa and the timing of entering into any new strategic collaboration with others relating to the

commercialization of Vascepa, if at all, and the terms of any such collaboration;

• continued costs associated with litigation and other legal proceedings;

• the time and costs involved in obtaining additional regulatory approvals for Vascepa based on REDUCE-IT results;

• 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 we require additional funds and adequate funds are not available to us in amounts or on terms acceptable to us or on a timely basis, or at all, our commercialization efforts for Vascepa may suffer materially.

The potential future benefit of our substantial net operating loss carryforwards could be lost and our prospects for profitability could be materially diminished if tax regulations or rates change or if we are deemed to not have active operations in Ireland.

Tax law and policies in the United States and Ireland are subject to change based on adjustments in political perspectives. In the United States and internationally, how to tax entities with international operations, like Amarin, has been subject to significant re-evaluation. We developed Vascepa in and from Ireland. In recent years, particularly since 2013 when commercial sale of Vascepa commenced in the United States, the majority of our consolidated operations have been in the United States. Ownership to Vascepa continues to reside with our wholly-owned Ireland-based subsidiary, Amarin Pharmaceuticals Ireland Ltd., and oversight and operations of that entity are structured to be maintained in Ireland. In order to effectively utilize our accumulated net operating loss carryforwards for tax purposes in Ireland, our operations, particularly for this subsidiary, need to be active in Ireland. In addition, utilization of these accumulated net operating loss carryforwards assumes that tax treaties between Ireland and other countries, particularly the United States, do not change in a manner which limit our future ability to offset earnings with these operating loss carryforwards for tax purposes.

Similarly, a change in our Irish tax residence could materially affect our ability to obtain profitability, if at all. Changes in tax law and tax rates, particularly in the United States and Ireland, could also impact our assessment of deferred taxes. Any change in our assessment of the realizability or the timing for realizing deferred taxes could have a negative impact our future profitability.

Continued negative economic conditions would likely have a negative effect 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 December 2012 Purchase and Sale Agreement with CPPIB Credit Europe S.à r.l., or CPPIB, as successor in interest to BioPharma Secured Debt Fund II Holdings Cayman LP, 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 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.

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. For example, in March 2014, we entered into a co-promotion agreement with Kowa Pharmaceuticals America, Inc. related to the commercialization of Vascepa in the United States. 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 February 22, 2019, we had 329,321,488 common shares outstanding including 329,087,415 shares held as ADSs and 234,073 held as ordinary shares (which are not held in the form of 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 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:

- developments or disputes concerning ongoing patent prosecution efforts and any future patent or proprietary rights;
- litigation and regulatory developments in the United States affecting our Vascepa promotional rights, and regulatory developments in other countries;
- actual or potential medical results relating to our products or our competitors' products;
- interim failures or setbacks in product development;
- innovation by us or our competitors;
- currency exchange rate fluctuations; and
- period-to-period variations in our results of operations.

The number of our ordinary shares, or ADSs representing such ordinary shares, outstanding may increase substantially as a result of our March 2015 private placement and the later consolidation and redesignation of the Series A Preference Shares represented by Preference ADSs issued thereunder, and some of the investors may then beneficially own significant blocks of our ordinary shares; the ordinary shares and Series A Preference Shares resulting from the private placement will be generally available for resale in the public market upon registration under the Securities Act.

In March and July 2015, we completed a private placement of American Depositary Shares in two tranches representing 352,150,790 and 38,867,180 Series A Preference Shares, respectively, each ten (10) of which may be consolidated and redesignated into one (1) ordinary share in our capital. During the three months ended June 30, 2015, 62,833,330 preferred shares were converted, resulting in the issuance of 6,283,333 ordinary shares and during the three months ended September 30, 2018, 38,867,180 preferred shares were converted, resulting in the issuance of 3,886,718 ordinary shares. The consolidation and redesignation of the Series A Preference Shares currently outstanding would result in an additional 28,931,746 ordinary shares outstanding, resulting in substantial dilution to shareholders who held our ordinary shares or ADSs representing such ordinary shares prior to the private placement. Although the Series A Preference Shares do not have voting rights, in general, upon consolidation and redesignation into ordinary shares some of the investors in the private placement could then have significant influence over the outcome of any shareholder vote, including the election of directors and the approval of mergers or other business combination transactions.

Pursuant to the securities subscription agreements that we entered into with the investors in the private placement, we agreed to file with the SEC a registration statement to register the resale of the Series A Preference Shares represented by American Depositary Shares issued in the private placement and the ordinary shares issuable upon the

consolidation and consolidation and redesignation of such Series A Preference Shares. Upon such registration and subsequent consolidation and redesignation, these securities will become generally available for immediate resale in the public market. The market price of our ordinary shares could fall as a result of an increase in the number of shares available for sale in the public market.

Failure to comply with our obligations under the March 2015 securities subscription agreements could result in our becoming liable for damages to certain investors under these agreements, including specified liquidated damages, which could be material in amount.

Under the terms of the March 2015 securities subscription agreements, we are subject to various obligations, failure to comply with which could result in our becoming liable to certain investors under these agreement for damages, which could be material in amount.

For example, under each of these agreements we have agreed to file and maintain the effectiveness of certain resale registration statements for ADSs representing the ordinary shares underlying the Series A Preference shares we issued and sold under these

agreements. Specifically, we have agreed to pay liquidated damages to the investors in the respective private placements if (a) the applicable resale registration statements we are required to file are not declared effective within 120 days after the closing of the applicable private placement, or (b) after effectiveness and subject to certain specified exceptions, we suspend the use of the applicable registration statement or the registration statement ceases to remain continuously effective as to all the securities for which it is required to be effective. We refer to each of these events as a registration default. Subject to the specified exceptions, for each 30-day period or portion thereof during which a registration default remains uncured, we are obligated to pay liquidated damages to each investor in cash in an amount equal to 1% of the aggregate subscription price paid by each such investor in the private placement, up to a maximum of 8% of such aggregate subscription price. These amounts could be material, and any liquidated damages we are required to pay could have a material adverse effect on our financial condition.

In addition, under the securities subscription agreement dated as of March 5, 2015, we are required to not publicly disclose the identity of the investors party to that agreement, subject to certain exceptions for disclosures required in securities filings and under applicable law. If we fail to comply with these obligations we could become liable to these investors for damages, including specified liquidated damages. For example, following certain public statements made by us on a quarterly conference call concerning the 2015 private placement, we agreed to specified liquidated damages in the event we are found to have violated the confidentiality provisions of the subscription agreement in the future.

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 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 is prudent to assume that we were classified as a PFIC in the past. However, we do not believe that we have been classified as a PFIC beginning in 2013 when we commercially launched Vascepa in the United States and began to derive revenues from sales of Vascepa. Our status as a PFIC is subject to change in future years.

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. 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 December 2012 Purchase and Sale Agreement could adversely affect our financial results and liquidity.

Pursuant to our December 2012 Purchase and Sale Agreement with CPPIB, which was assigned to CPPIB by BioPharma Secured Debt Fund II Holdings Cayman LP in December 2017, we are obligated to make payments 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 CPPIB'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 CPPIB.

Upon a transaction resulting in a change of control of Amarin, as defined in the agreement, CPPIB 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 CPPIB and (iii), unless CPPIB has been paid a certain amount under the indebtedness, certain licensings 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 shareholders.

To secure our obligations under the agreement, we granted CPPIB 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 CPPIB 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 indebtedness could adversely affect our financial condition.

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

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 of 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 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.

Shareholder protections found in provisions under the U.K. City Code on Takeovers and Mergers, or the Takeover Code, do not apply to us.

The Takeover Code provides a framework within which takeovers of certain companies organized in the United Kingdom are regulated and conducted. However, because our place of central management and control is currently outside of the United Kingdom, we are not subject to the Takeover Code. As a result, our shareholders are not entitled to the benefit of certain takeover offer protections provided under the Takeover Code. The following is a brief summary of some of the most important rules of the Takeover Code which, as noted, does not apply to us:

In connection with a potential offer, if following an approach by or on behalf of a potential bidder, the company is “the subject of rumor or speculation” or there is an “untoward movement” in the company’s share price, there is a requirement for the potential bidder to make a public announcement about a potential offer for the company, or for the company to make a public announcement about its review of a potential offer.

When a person or group (a) acquires interests in shares carrying 30% or more of the voting rights of a company (which percentage is treated by the Takeover Code as the level at which effective control is obtained) or (b) increases the aggregate percentage interest they have when they are already interested in not less than 30% and not more than 50%, they must make a cash offer to all other shareholders at the highest price paid by them in the 12 months before the offer was announced.

When interests in shares carrying 10% or more of the voting rights of a class have been acquired by an offeror (i.e., a bidder) in the offer period (i.e., before the shares subject to the offer have been acquired) and the previous 12 months,

the offer must be in cash or be accompanied by a cash alternative for all shareholders of that class at the highest price paid by the offeror in that period. Further, if an offeror acquires any interest in shares during the offer period, the offer for the shares must be in cash or accompanied by a cash alternative at a price at least equal to the price paid for such shares during the offer period.

• If after an announcement is made, the offeror acquires an interest in shares in an offeree company (i.e., a target) at a price higher than the value of the offer, the offer must be increased accordingly.

• The offeree company must appoint a competent independent adviser whose advice on the financial terms of the offer must be made known to all the shareholders, together with the opinion of the board of directors of the offeree company.

• Favorable deals for selected shareholders are not permitted, except in certain circumstances where independent shareholder approval is given and the arrangements are regarded as fair and reasonable in the opinion of the financial adviser to the offeree.

• All shareholders must be given the same information.

• Those issuing takeover circulars must include statements taking responsibility for the contents thereof.

• Profit forecasts, quantified financial benefits statements and asset valuations must be made to specified standards and must be reported on by professional advisers.

• Misleading, inaccurate or unsubstantiated statements made in documents or to the media must be publicly corrected immediately.

• Actions during the course of an offer by the offeree company, which might frustrate the offer are generally prohibited unless shareholders approve these plans. Frustrating actions would include, for example, lengthening the notice period for directors under their service contract or agreeing to sell off material parts of the target group.

• Stringent requirements are laid down for the disclosure of dealings in relevant securities during an offer, including the prompt disclosure of positions and dealing in relevant securities by the parties to an offer and any person who is interested (directly or indirectly) in 1% or more of any class of relevant securities.

- Employees of both the offeror and the offeree company and the trustees of the offeree company's pension scheme must be informed about an offer. In addition, the offeree company's employee representatives and pension scheme trustees have the right to have a separate opinion on the effects of the offer on employment appended to the offeree board of directors' circular or published on a website.

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.

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.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

The following table lists the location, use and ownership interest of our principal properties as of February 22, 2019:

Location	Use	Ownership	Size (sq. ft.)
Dublin, Ireland	Offices	Leased	270
Bedminster, New Jersey, USA	Offices	Leased	27,951

Effective November 1, 2011, we leased 320 square feet of office space in Dublin, Ireland. The office space was subsequently reduced to 270 square feet, effective November 1, 2013. The lease terminates on October 31, 2019 and may be renewed annually.

Effective July 1, 2011, we leased 9,747 square feet of office space in Bedminster, New Jersey. On December 6, 2011 we leased an additional 2,142 square feet of space in the same location. On December 15, 2012 and May 8, 2013, we leased an additional 2,601 and 10,883 square feet of space, respectively, in the same location. In January 2014 and April 2014, we entered into separate transactions with the landlord of this property to vacate approximately 2,142 and 2,000 square feet of space in exchange for discounts on contractual future rent payments. In January 2015, we signed an agreement to sublease approximately 4,700 square feet of this property to a third party, effective April 1, 2015. This sublease agreement was terminated as of September 30, 2017. Additionally, in June 2015, we executed an agreement to sublease approximately 2,500 square feet of this property to a separate third party, effective June 16, 2015, which agreement naturally ceased on March 31, 2018. On December 15, 2016, we leased an additional 732 square feet of space in the same location, effective January 1, 2017. The lease, as amended, terminates on April 30, 2019, but we are currently in the process of extending this lease through the start of the new Bridgewater, New Jersey lease, as described below. On January 26, 2019, we leased an additional 5,988 square feet in an annex building, effective February 1, 2019 and terminating June 30, 2019.

As described more fully in Note 17—Subsequent Events, given the anticipated expiration in 2019 of the lease described above, on February 5, 2019, we entered into a lease agreement for approximately 67,747 square feet of office space in Bridgewater, New Jersey with a commencement date anticipated to be on or about July 1, 2019, which will better suit our needs going forward. We believe that our existing facilities and disclosed plans for new facilities are adequate for our current needs and that additional space will be available in the future on commercially reasonable terms as needed.

Item 3. Legal Proceedings

On February 22, 2019, a purported investor in our publicly traded securities filed a putative class action lawsuit against Amarin Corporation plc, our chief executive officer and chief scientific officer in the U.S. District Court for the District of New Jersey, *Debendra Sharma v. Amarin Corporation plc, John F. Thero and Steven Ketchum*, No. 2:19-cv-06601 (D.N.J. Feb. 22, 2019). The lawsuit alleges that, during the period September 24, 2018 and November 9, 2018, we misled investors by purportedly not disclosing that the placebo given to patients in the REDUCE-IT study, mineral oil, may have caused cardiovascular problems in the patients taking it, thereby misleading investors on the outcome of the REDUCE-IT study and artificially inflating the price of our securities. Based on these allegations, the suit asserts claims under the Securities Exchange Act of 1934 and seeks unspecified monetary damages and attorneys' fees and costs. We believe that we have valid defenses and we will vigorously defend against the claims, but cannot predict the outcome of this lawsuit. We are unable to reasonably estimate the loss exposure, if any, associated with the claims. We have insurance coverage that is anticipated to cover any significant loss exposure that may arise from this action after payment by us of the associated deductible obligation under such insurance coverage.

On August 30, 2017, Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited, each wholly-owned subsidiaries of Amarin Corporation plc, filed a lawsuit with the United States International Trade Commission, or the ITC, captioned *In the Matter of Certain Synthetically Produced, Predominantly EPA Omega-3 Products in Ethyl Ester or Re-esterified Triglyceride Form*, USITC Docket 337-3247, against manufacturers, importers, and distributors of products containing synthetically produced omega-3 products in ethyl ester or re-esterified triglyceride form that contain more EPA than DHA or any other single component for use in or as dietary supplements. The lawsuit sought an investigation by the ITC under Section 337 of the Tariff Act of 1930 (19 U.S.C. §1337), which makes unlawful unfair methods of competition and unfair acts involving the importation and sale of articles in the United States that injure or threaten injury to a domestic industry. On October 27, 2017, the ITC determined to not institute our requested investigation. On December 1, 2017, we appealed the ITC's non-institution decision to the United States Court of Appeals for the Federal Circuit (Case Nos. 18-1247, 18-114). That appeal is ongoing. We intend to pursue this matter vigorously.

In September and October 2016, we received paragraph IV certification notices from four companies contending to varying degrees that certain of our patents are invalid, unenforceable and/or will not be infringed by the manufacture,

use, sale or offer for sale of a generic form of Vascepa as described in those companies' abbreviated new drug applications, or ANDAs. We filed patent infringement lawsuits against three of these four ANDA applicants. In October 2016, Amarin filed a lawsuit against Roxane Laboratories, Inc. and related parties (collectively, "Roxane") in the U.S. District Court for the District of Nevada. The case against Roxane is captioned Amarin Pharma, Inc. et al. v. Roxane Laboratories, Inc. et al., Civ. A. No. 2:16-cv-02525 (D. Nev.). According to a stipulation filed with the Nevada court, in December 2016, Roxane transferred its ANDA to West-Ward Pharmaceuticals International Limited, which then designated West-Ward Pharmaceuticals Corp. (or together with West-Ward Pharmaceuticals International Limited, West-Ward) as its agent for FDA communications. In view of the ANDA transfer, in February 2017, West-Ward replaced Roxane and related parties as Defendants in the above-referenced case. The case against West-Ward is now captioned Amarin Pharma, Inc. et al. v. West-Ward Pharmaceuticals Corp. et al., Civ. A. No. 2:16-cv-02525 (D. Nev.). In November 2016, Amarin filed a lawsuit against Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd. (collectively, "DRL") in the U.S. District Court for the District of Nevada. The case against DRL is captioned Amarin Pharma, Inc. et al. v. Dr. Reddy's Laboratories, Inc. et al., Civ. A. No. 2:16-cv-02562 (D. Nev.). In November 2016, Amarin filed a lawsuit against Teva Pharmaceuticals USA, Inc. and Teva Pharmaceuticals Industries Limited (collectively, "Teva") in the U.S. District Court for the District of Nevada. The case against Teva is captioned Amarin Pharma, Inc. et al. v. Teva Pharmaceuticals USA, Inc. et al., Civ. A. No. 2:16-cv-02658. In all three lawsuits, Amarin is seeking, among other remedies, an order enjoining each defendant from marketing generic versions of Vascepa

before the last to expire of the asserted patents in 2030. The three lawsuits have been consolidated for pretrial proceedings. As a result of the statutory stay associated with the filing of these lawsuits under the Hatch-Waxman Act, the FDA cannot grant final approval to West-Ward, DRL, or Teva's respective ANDA before January 2020, unless there is an earlier court decision holding that the subject patents are not infringed and/or are invalid.

The fourth ANDA applicant referenced above is Apotex Inc. ("Apotex"), which sent Amarin a paragraph IV certification notice in September 2016. The notice reflected that Apotex made a paragraph IV notice as to some, but not all, of the patents listed in the Orange Book for Vascepa. Because Apotex did not make a paragraph IV certification as to all listed patents, Apotex cannot market a generic version of Vascepa before the last to expire of the patents for which Apotex did not make a paragraph IV certification, which is in 2030. At a later date, Apotex may elect to amend its ANDA in order to make a paragraph IV certification as to additional listed patents. If and when Apotex does make such an amendment, it would be required to send Amarin an additional paragraph IV certification notice, and Amarin would then have the ability to file a lawsuit against Apotex pursuant to the Hatch-Waxman Act.

In October 2016, we introduced to the market a 0.5-gram dose strength of Vascepa. In August 2017, as anticipated, we received a paragraph IV certification notice from Teva contending that certain of our patents are invalid, unenforceable and/or will not be infringed by the manufacture, use, sale or offer for sale of a generic form of the 0.5-gram dose strength of Vascepa, as described in the Teva ANDA. This Teva ANDA was filed as an amendment to the 1-gram Teva ANDA and is related to patents already at issue in the 1-gram Vascepa patent litigation. This certification followed the related listing in the Orange Book of patents associated with the 0.5-gram product in June 2017. This June 2017 listing was within the five-year, post NDA-approval period during which the Hatch-Waxman Amendments require a paragraph IV certification of patent invalidity or non-infringement under the Hatch-Waxman, five-year, NCE regulatory scheme. Accordingly, in October 2017, we filed a patent infringement lawsuit against Teva in the U.S. District Court for the District of Nevada. The case is captioned Amarin Pharma, Inc. et al. v. Teva Pharmaceuticals USA, Inc. et al., Civ. A. No. 2:17-cv-2641 (D. Nev.). In this lawsuit, we sought, among other remedies, an order enjoining Teva from marketing generic versions of the 0.5-gram dose strength of Vascepa before the last to expire of the asserted patents in 2030.

On May 24, 2018, we entered into a settlement agreement with Teva that resolves our ANDA patent litigation as it relates to Teva's as amended ANDA for both the 1-gram and 0.5-gram dose strengths of Vascepa. As part of this settlement agreement, Teva may first begin selling its generic version of Vascepa in the United States on August 9, 2029, or earlier under certain customary circumstances, including commercial launch by another generic manufacturer under certain circumstances, in which event Teva would pay us certain royalties on its generic Vascepa products. The ANDA patent litigation continues in the United States District Court for the District of Nevada with parties West-Ward and DRL.

In July 2018, as anticipated, we received a paragraph IV certification notice from DRL contending that certain of our patents are invalid, unenforceable and/or will not be infringed by the manufacture, use, sale or offer for sale of a generic form of the 0.5-gram dose strength of Vascepa, as described in the DRL ANDA. This DRL ANDA was filed as an amendment to the 1-gram DRL ANADA and is related to patents already at issue in the 1-gram Vascepa patent litigation. This certification followed the related listing in the Orange Book of patents associated with the 0.5-gram product in June 2017. This June 2017 listing was within the five-year, post NDA-approval period during which the Hatch-Waxman Amendments require a paragraph IV certification of patent invalidity or non-infringement lawsuit against DRL in the U.S. District Court for the District of Nevada. The case is captioned Amarin Pharma, Inc. et al. v. Dr. Reddy's Laboratories, Inc. et al., Civ. A. No. 2:18-cv-01596 (D. Nev.). In this lawsuit, we are seeking, among other remedies, an order enjoining DRL from marketing generic versions of the 0.5-gram dose strength of Vascepa before the last to expire of the asserted patents in 2030. In light of the overlap between the cases, DRL and Amarin have stipulated that the final judgment on the merits of the parties' contentions in the consolidated 1-gram action shall also be binding in the 0.5-gram case.

We intend to vigorously enforce our intellectual property rights relating to Vascepa, but we cannot predict the outcome of these lawsuits or any subsequently filed lawsuits.

In addition to the above, in the ordinary course of business, we are from time to time involved in lawsuits, claims, investigations, proceedings, and threats of litigation relating to intellectual property, commercial arrangements and other matters.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

The following table sets forth the high and low prices for our ADSs in each of the quarters over the past two fiscal years, as quoted on The NASDAQ Global Market under the symbol “AMRN.”

	Common Stock Price			
	Fiscal 2018		Fiscal 2017	
	High	Low	High	Low
First Quarter	\$4.60	\$2.91	\$3.58	\$2.81
Second Quarter	\$3.52	\$2.66	\$4.10	\$2.85
Third Quarter	\$16.34	\$2.35	\$4.47	\$2.97
Fourth Quarter	\$23.34	\$11.78	\$4.24	\$3.04

Shareholders

As of January 31, 2019, there were approximately 360 holders of record of our ordinary shares. Because many ordinary shares are held by broker nominees, we are unable to estimate the total number of shareholders represented by these record holders. Our depository, Citibank, N.A., constitutes a single record holder of our ordinary shares.

Dividends

We have never paid dividends on common shares and do not anticipate paying any cash dividends on the common 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 stockholders, and may only be paid from our distributable profits available for the purpose, determined on an unconsolidated basis.

Under our Purchase and Sale Agreement with CPPIB Credit Europe S.à r.l., or CPPIB, as successor in interest to BioPharma Secured Debt Fund II Holdings Cayman LP, we are restricted from paying a dividend on our common shares, unless we have cash and cash equivalents in excess of a specified amount after such payment.

Performance Graph—5 Year

The following performance graph and related information shall not be deemed “soliciting material” or to be “filed” with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the cumulative 5-year return provided to stockholders of Amarin’s ADSs relative to the cumulative total returns of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. We believe these indices are the most appropriate indices against which the total shareholder return of Amarin should be measured. The NASDAQ Biotechnology Index has been selected because it is an index of U.S. quoted biotechnology and

pharmaceutical companies. An investment of \$100 (with reinvestment of all dividends) is assumed to have been made in our ADSs and in each of the indices on January 1, 2014 and its relative performance is tracked through December 31, 2018.

Included in this 5-year time period is the substantial positive impact on the price of Amarin's ADSs following presentation and publication of positive REDUCE-IT results in 2018.

Company/Market/Peer Company	12/31/2014	12/31/2015	12/31/2016	12/31/2017	12/31/2018
Amarin Corporation PLC	\$ 50.25	\$ 96.48	\$ 154.77	\$ 201.51	\$ 683.92
NASDAQ Composite Index	\$ 116.34	\$ 122.18	\$ 130.28	\$ 167.08	\$ 160.59
NASDAQ Biotechnology Index	\$ 135.80	\$ 150.53	\$ 117.41	\$ 142.13	\$ 128.88

Performance Graph—3 Year

The following performance graph and related information shall not be deemed “soliciting material” or to be “filed” with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the cumulative 3-year return provided to stockholders of Amarin's ADSs relative to the cumulative total returns of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. We believe these indices are the most appropriate indices against which the total shareholder return of Amarin should be measured. The NASDAQ Biotechnology Index has been selected because it is an index of U.S. quoted biotechnology and pharmaceutical companies. An investment of \$100 (with reinvestment of all dividends) is assumed to have been made in our ADSs and in each of the indices on January 1, 2016 and its relative performance is tracked through December 31, 2018.

Included in this 3-year time period is the substantial positive impact on the price of Amarin's ADSs in 2018 following presentation and publication of positive REDUCE-IT results. During this entire 3-year time period, cumulative total return for Amarin's ADSs exceeded both the NASDAQ Composite Index and NASDAQ Biotechnology Index.

Company/Market/Peer Company	12/31/2016	12/31/2017	12/31/2018
Amarin Corporation PLC	\$ 162.96	\$ 212.17	\$ 720.11
NASDAQ Composite Index	\$ 107.50	\$ 137.86	\$ 132.51
NASDAQ Biotechnology Index	\$ 78.32	\$ 94.81	\$ 85.97

Information about Our Equity Compensation Plans

Information regarding our equity compensation plans is incorporated by reference in Item 12 of Part III of this annual report on Form 10-K.

Unregistered Sales of Equity Securities and Use of Proceeds

Issuer Purchases of Equity Securities

Shares purchased in the fourth quarter of 2018 are as follows:

Period	Total Number of	Average Price
	Shares Purchased ⁽¹⁾	Paid per Share
October 1 – 31, 2018	—	\$ —
November 1 – 30, 2018	—	—
December 1 – 31, 2018	41,252	13.24
Total	41,252	\$ 13.24

(1) Represents shares withheld to satisfy tax withholding amounts due from employees related to the receipt of stock which resulted from the exercise or vesting of equity awards.

UNITED KINGDOM TAXATION

Capital Gains

If you are not resident in the United Kingdom, or UK, for UK tax purposes, you will not be liable for UK tax on capital gains realized or accrued on the sale or other disposition of common shares or ADSs unless the common shares or ADSs are held in connection with your trade carried on in the UK through a branch or agency and the common shares or ADSs are or have been used, held or acquired for the purposes of such trade or such branch or agency.

An individual holder of common shares or ADSs who ceases to be resident in the UK for UK tax purposes for a period of less than 5 years and who disposes of common shares or ADSs during that period may also be liable on returning to the UK for UK capital gains tax despite the fact that the individual may not be resident in the UK at the time of the disposal.

Inheritance Tax

If you are an individual domiciled in the United States and are not a national of the UK for the purposes of the Inheritance and Gift Tax Treaty 1978 between the United States and the UK, any common shares or ADSs beneficially owned by you will not generally be subject to UK inheritance tax on your death or on a gift made by you during your lifetime, provided that any applicable United States federal gift or estate tax liability is paid, except where the common share or ADS is part of the business property of your UK permanent establishment.

Where the common shares or ADSs have been placed in trust by a settlor who, at the time of the settlement, was domiciled in the United States and not a national of the UK, the common shares or ADSs will not generally be subject to UK inheritance tax.

Stamp Duty and Stamp Duty Reserve Tax

Transfer of ADSs

No UK stamp duty will be payable on an instrument transferring an ADS or on a written agreement to transfer an ADS provided that the instrument of transfer or the agreement to transfer is executed and remains at all times outside the UK. Where these conditions are not met, the transfer of, or agreement to transfer, an ADS could, depending on the circumstances, attract a charge to ad valorem stamp duty at the rate of 0.5% of the value of the consideration.

No stamp duty reserve tax will be payable in respect of an agreement to transfer an ADS, whether made in or outside the UK.

Issuance and Transfer of Common Shares

The issuance of common shares by Amarin will not give rise to a charge to UK stamp duty or stamp duty reserve tax under current UK and European Union law; it is not currently known whether this position will continue for UK stamp duty reserve tax in relation to the issuance of common shares in return for an issuance of ADSs after the United Kingdom leaves the European Union. In the event of a change in this position resulting in the issuance of common shares by Amarin giving rise to a charge to UK stamp duty or stamp duty reserve tax, Amarin would be responsible for any such UK stamp duty reserve tax payable on the issuance of common shares in return for the issuance of ADSs.

Transfers of common shares, as opposed to ADSs, will attract ad valorem stamp duty at the rate of 0.5% of the amount or value of the consideration. A charge to stamp duty reserve tax, at the rate of 0.5% of the amount or value of the consideration, will arise on an agreement to transfer common shares. The stamp duty reserve tax is payable on the seventh day of the month following the month in which the charge arises. Where an instrument of transfer is executed and duly stamped before the expiry of a period of six years beginning with the date of that agreement, any stamp duty reserve tax that has not been paid ceases to be payable.

Taxation of Dividends

Under UK law, there is no withholding tax on dividends paid on the common shares or ADSs.

Item 6. Selected Financial Data

The selected financial data set forth below as of and for the years ended December 31, 2018, 2017, 2016, 2015, and 2014 have been derived from the audited consolidated financial statements of Amarin. This data should be read in conjunction with our audited consolidated financial statements and related notes which are included elsewhere in this Annual Report on Form 10-K, and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in Item 7 below. Historical results are not necessarily indicative of operating results to be expected in the future.

	Years Ended December 31,				
	2018	2017	2016	2015	2014
	(In thousands, except per share amounts)				
Consolidated Statements of Operations Data:					
Product revenue, net	\$228,371	\$179,825	\$128,966	\$80,987	\$54,202
Licensing revenue	843	1,279	1,118	769	—
Total revenue, net	229,214	181,104	130,084	81,756	54,202
Less: Cost of goods sold	54,543	44,952	34,363	27,875	20,485
Gross margin	174,671	136,152	95,721	53,881	33,717
Operating expenses:					
Selling, general and administrative (1)	226,996	134,549	111,372	101,041	79,346
Research and development	55,900	47,158	49,975	51,062	50,326
Total operating expenses	282,896	181,707	161,347	152,103	129,672
Operating loss	(108,225)	(45,555)	(65,626)	(98,222)	(95,955)
Gain (loss) on change in fair value of derivative liabilities (2)	—	—	8,170	(1,106)	13,472
Gain on extinguishment of debt	—	—	—	1,314	38,034
Interest expense	(8,872)	(9,766)	(18,677)	(20,180)	(18,575)
Interest income	1,074	429			