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MEDICINES CO /DE

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As Filed Pursuant to Rule 424(b)(5)
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The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, Dated June 24, 2019

Preliminary Prospectus Supplement
(to Prospectus Dated June 24, 2019)

$150,000,000

THE MEDICINES COMPANY

Common Stock

We are offering $150,000,000 of shares of our common stock.

Our common stock trades on the NASDAQ Global Select Market under the trading symbol "MDCO". On June 21, 2019, the last sale price of our common stock as reported on the NASDAQ Global Select Market was $36.40 per share.

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions	$	$
Proceeds, before expenses, to us	$	$

We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to an additional $22,500,000 of shares of our common stock at the public offering price, less the underwriting discounts and commissions.

Investing in our common stock involves risks. See "Risk Factors" beginning on page S-10 of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares to the purchasers on or about June , 2019.

Joint Book-Running Managers

Goldman Sachs & Co. LLC **J.P. Morgan**

June , 2019

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Prospectus Supplement

Prospectus

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein or therein is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled "Where you can find more information" and "Incorporation of certain information by reference" in this prospectus supplement and in the accompanying prospectus.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

The Medicines Company® name and logo are either registered trademarks or trademarks of The Medicines Company in the United States and/or other countries. All other trademarks, service marks or other tradenames appearing herein are the property of their respective owners. References to the Company, "we," "us" or "our" mean The Medicines Company, a Delaware corporation, and its subsidiaries.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). For this purpose, any statements contained or incorporated by reference herein regarding our company, this offering, the securities offered hereby, our strategy, future operations, financial position, liquidity, future revenue, projected costs, prospects, plans and objectives of management, other than statements of historical facts, are forward-looking statements. The words "anticipates," "believes," "estimates," "expects," "intends," "may," "plans," "projects," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations expressed or implied in our forward-looking statements. There are a number of important factors that could cause actual results, levels of activity, performance or events to differ materially from those expressed or implied in the forward-looking statements we make. These important factors include our "critical accounting estimates" described in Part II, Item 7 "Management's Discussion and Analysis of Financial Condition and Results of Operations—Application of Critical Accounting Estimates" of our Annual Report on Form 10-K for the fiscal year ended December 31, 2018 and Part I, Item 2 of our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2019, each of which is incorporated herein by reference; and the factors set forth under "Risk Factors" beginning on page S-10 of this prospectus supplement.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the risks of investing in our common stock discussed under "Risk Factors" beginning on page S-10 of this prospectus supplement, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.

The Medicines Company

Our Business

We are a biopharmaceutical company driven by our purpose to solve major medical, societal and economic challenges in healthcare. We have a singular focus on one of the greatest global healthcare challenges and burdens—that presented by atherosclerotic cardiovascular disease ("ASCVD"), which remains the number one cause of death in the United States and worldwide. We take on that challenge by developing inclisiran, the investigational RNA interference ("RNAi") therapeutic, that specifically inhibits production of proprotein convertase subtilisin/kexin type 9 ("PCSK9"), a key protein that controls LDL-cholesterol ("LDL-C") levels. We believe inclisiran is uniquely suited to make a significant difference reducing risk in ASCVD. We have the right to develop, manufacture and commercialize inclisiran under our collaboration agreement with Alnylam Pharmaceuticals, Inc. ("Alnylam").

On August 22, 2018, we completed the sale of our rights to branded Angiomax in the United States to Sandoz Inc. ("Sandoz"), for $9.9 million. Following such divestiture, we no longer market any products. Historically, our revenues have been generated primarily from sales of Angiomax in the United States, but competition from generic versions of Angiomax following the loss of market exclusivity in the United States in July 2015 and in Europe in August 2015 resulted in a significant decline in revenue from Angiomax prior to our divestiture of the product. Based on our current business, we expect to incur net losses for the foreseeable future.

Inclisiran

Overview

Inclisiran is a subcutaneously administered small interfering RNA ("siRNA"), that prevents the production of PCSK9 and is being developed as a potential treatment for hypercholesterolemia. siRNA therapy harnesses a natural mechanism called RNAi. We obtained global rights to this product candidate under a license and collaboration agreement that we entered into with Alnylam in February 2013 to develop, manufacture and commercialize RNAi therapeutics targeting the PCSK9 gene for the treatment of hypercholesterolemia and other human diseases. RNAi is a natural mechanism within cells to selectively prevent the production of specific proteins. PCSK9 is a protein involved in the regulation of low-density lipoprotein ("LDL"), receptor levels on cells in the liver (hepatocytes) responsible for cholesterol clearance. Inclisiran prevents the production of PCSK9 and lowers LDL-C levels.

PCSK9 and PCSK9 inhibition

PCSK9, a member of the serine protease family, plays a key role in controlling the levels of LDL receptors on the surface of certain liver cells called hepatocytes. PCSK9 is expressed and secreted into the bloodstream predominantly by the liver, binds LDL receptors both intracellularly and extracellularly and promotes the lysosomal degradation of these receptors in hepatocytes. By reducing the available

LDL receptor pool on the surface of hepatocytes, PCSK9 increases circulating LDL-C levels. People with naturally occurring variants in the PCSK9 gene and consequently lower PCSK9 protein activity have reduced serum LDL-C levels and lower risk for coronary heart disease, with no apparent negative health consequences.

RNA interference

RNAi is a natural process within cells to prevent the production of specific proteins and represents a promising aspect of biology and drug development today. Its discovery was recognized with the award of the 2006 Nobel Prize for Physiology or Medicine. siRNAs are the molecules that mediate RNAi within cells, and siRNA therapies such as inclisiran harness the natural RNAi process. siRNAs function upstream of today's medicines by targeting the root cause of diseases. This approach has the potential to transform the care of patients.

Clinical Development

Overview

Under our global license and collaboration agreement with Alnylam, we and Alnylam initially collaborated on the development of inclisiran and ALN-PCS02, an intravenously administered earlier siRNA therapy. Alnylam was responsible for the development of these product candidates until Phase 1 was completed. We have assumed the responsibility for the further development and commercialization of all product candidates under our agreement with Alnylam. In October 2013, we and Alnylam selected a lead subcutaneously administered development candidate, now referred to as inclisiran, for development for the potential to lower LDL-C. In December 2014, under the terms of our agreement with Alnylam, Alnylam initiated a Phase 1 clinical trial of inclisiran in the United Kingdom. Data from the Phase 1 trial was presented at the European Society of Cardiology meeting in August 2015 and at the American Heart Association meeting in November 2015, and was published in the New England Journal of Medicine.

In January 2016, we began enrolling patients in the ORION-1 Phase 2 dose finding trial. ORION-1 was a placebo-controlled, double-blind, randomized trial of single or multiple subcutaneous injections of inclisiran in a total of 501 patients with ASCVD or ASCVD-risk equivalents (e.g., diabetes and familial hypercholesterolemia), and elevated LDL-C despite maximally tolerated LDL-C lowering therapies. The study compared the effect of different doses of inclisiran and evaluated the potential for an infrequent dosing regimen. The primary endpoint of the study was the percentage change in LDL-C from baseline at Day 180.

In March 2017, we reported positive final results from the ORION-1 Phase 2 study of inclisiran. Efficacy data presented reaffirmed inclisiran's significant LDL-C lowering effects. Administration of 284 mg of inclisiran (300 mg inclisiran sodium) on Day-1 and Day-90 lowered the mean LDL-C by an average of 52.6% and up to 81% at Day-180. For the subsequent six-month period, from Day-90 to Day-270, the time-averaged LDL-C reduction was 51%. These robust data underscore the potential of a six-monthly maintenance regimen, which is currently being evaluated in the inclisiran Phase 3 clinical program. No material safety issues were observed on inclisiran in ORION-1, which demonstrated an adverse event profile similar to placebo.

We developed a dose-pharmacodynamic ("dose-PD"), response model based on the ORION-1 data to perform modeling and simulation experiments to support the selection of the Phase 3 dose and dose regimen. The dose-PD modeling and simulation supported the clinical observations from ORION-1 that a 300 mg dose given subcutaneously on Day-1, Day-90 and every six months thereafter is the optimal dose and dose regimen for further development in Phase 3. This dose and dose regimen maintains a time-averaged LDL-C reduction of >50%. Our initial Phase 3 program, described below, will test this dose and dose regimen in patients with ASCVD, ASCVD-risk equivalents, or familial

hypercholesterolemia ("FH"). Further dose-PD response modeling and simulation demonstrated that a 300 mg dose given once a year would result in a time-averaged LDL-C reduction of approximately 43-45%. We believe that this once a year dose regimen of 300 mg of inclisiran could be tested in patient populations at lower cardiovascular risk for whom daily oral tablets remain a challenge.

In January 2017, we initiated the ORION-2 and ORION-3 studies. ORION-2 is a pilot study to examine the efficacy, safety and tolerability of inclisiran in a limited number of patients with homozygous FH, to support further evaluation in the larger ORION-5 trial (described below). The ORION-3 study is an open label extension study of ORION-1 with the objective to evaluate the efficacy, safety and tolerability of long-term dosing of inclisiran. ORION-3 will also assess the feasibility of switching to inclisiran from evolocumab (trade named Repatha) on certain clinical and patient-reported endpoints.

In May 2019, we obtained new long-term data from the ORION-3 study, showing that twice-a-year dosing with inclisiran consistently resulted in more than 50% lower LDL cholesterol after 3 years. In addition, no material safety issues were observed with three years of follow-up in the study. ORION-3 shows no change in the overall safety profile compared to the one-year follow-up in ORION-1.

Phase 3 Clinical Program—ORION 5, 9, 10 and 11 clinical trials.

In the fourth quarter of 2017, we initiated the Phase 3 LDL-C lowering program for inclisiran. The Phase 3 program is comprised of four pivotal clinical trials in patients with ASCVD, ASCVD-risk equivalents, heterozygous FH, and homozygous FH. We anticipate that data from three trials, ORION-9, ORION-10 and ORION-11, will support the submission of a new drug application ("NDA"), in the United States and a marketing authorization application ("MAA"), in the European Union at or around the end of 2019. In the ORION-9, ORION-10 and ORION-11 trials, patients will be studied for 18 months and inclisiran 284 mg (inclisiran sodium 300 mg) will be given subcutaneously on Day-1, Day-90 and every six months thereafter for a total of four doses during the 18-month study period. As of June 20, 2019, more than 3,300 subjects had received a fourth dose of inclisiran or placebo in the ORION-9, ORION-10 and ORION-11 trials. We expect to start reporting Phase 3 data readouts in the second half of the third quarter of 2019. We expect patients in the ORION-5 trial of inclisiran in patients with homozygous FH to have a shorter comparative treatment window than the patients in the other ORION Phase 3 trials. The four Phase 3 clinical trials are further described below:

Study	Sites	Main inclusion criteria	Patients
ORION-5	US, EU, South Africa (SA)	Homozygous familial hypercholesterolemia ("HoFH")	45 (estimated)
ORION-9	US, EU, SA	Heterozygous familial hypercholesterolemia ("HeFH")	482
ORION-10	US	ASCVD	1,561
ORION-11	EU, SA	ASCVD and risk equivalent patients	1,617
			3,705

ORION-5 is a two-part (double-blind, placebo-controlled/open label) multicenter study to evaluate safety, tolerability, and efficacy of inclisiran in approximately 45 subjects with HoFH. We commenced enrollment in the ORION-5 trial in February 2019. On January 23, 2018, the U.S. Food and Drug Administration (the "FDA") granted orphan drug designation for inclisiran for the treatment of HoFH.

ORION-9 is a placebo-controlled, double-blind, randomized study of inclisiran versus placebo (1:1) in approximately 482 patients with HeFH. The primary endpoint of ORION-9 study is LDL-C reduction from baseline at Day-510. The ORION-9 trial commenced in November 2017. In February 2018, we announced that this trial had exceeded its target enrollment of 400 patients.

ORION-10 is a placebo-controlled, double-blind, randomized study of inclisiran versus placebo (1:1) in approximately 1,561 patients with ASCVD and LDL-C levels above 70 mg/dL despite maximum tolerated doses of LDL-C lowering therapies including statins. The primary endpoint of ORION-10 study is LDL-C reduction from baseline at Day-510. The ORION-10 trial commenced in November 2017 and in March 2018, we announced that this trial had exceeded its target enrollment of 1,500 patients.

ORION-11 is a placebo-controlled, double-blind, randomized study of inclisiran versus placebo (1:1) in approximately 1,617 patients with ASCVD or ASCVD-risk equivalents and elevated LDL-C levels above 70 mg/dL or 100 mg/dL, respectively, despite maximum tolerated doses of LDL-C lowering therapies including statins. The primary endpoint of the study is LDL-C reduction from baseline at Day-510. The ORION-11 trial commenced in November 2017. In January 2018, we announced that this trial had exceeded its target enrollment of 1,500 patients.

Cardiovascular Outcomes Trial—ORION-4

We are also conducting a cardiovascular outcomes trial in approximately 15,000 patients with ASCVD on a background of standard-of-care lipid-lowering therapy (usually high intensity statins), to determine the effects of inclisiran on cardiovascular outcomes. We initiated enrollment in the trial in October 2018. The overall design of the ORION-4 outcomes trial has been agreed to with the FDA and EMA. The ORION-4 study will be conducted in close collaboration with the academic groups, Clinical Trial Service Unit and Epidemiological Studies Unit of the University of Oxford and Thrombolysis In Myocardial Infarction (TIMI) Study Group of the Brigham and Women's Hospital, Boston, Massachusetts, as well as other scientific experts. The primary efficacy endpoint of the trial will be a composite endpoint of coronary heart disease death, non-fatal myocardial infarction, fatal or non-fatal ischemic stroke and urgent coronary revascularization. These endpoints have been demonstrated to be modifiable in previous, similar outcomes trials with lipid modifying therapies. The duration of the outcomes trial will be long enough, with a median of four to five years follow-up, to accumulate a sufficient number of events to ascertain treatment group differences and demonstrate the maximum clinical effect size associated with LDL-C lowering. We anticipate that, if inclisiran is approved for sale and the outcomes trial is successful, we will submit the results of the outcomes trial to the FDA as a supplemental New Drug Application ("sNDA"), and as a variation to the MAA with the European Medicines Agency ("EMA").

Medical Need

Despite advances in treatment, cardiovascular disease is the leading cause of death worldwide, resulting in over 18 million deaths annually. Eighty-five percent of all cardiovascular disease deaths are due to coronary heart disease or strokes. Not merely a disease of the elderly, cardiovascular disease is responsible for more than a third of the 17 million premature deaths annually worldwide, causing substantial losses in economic productivity.

Elevated LDL-C is the primary cause of ASCVD and the most readily modifiable risk factor, and of itself a major cause of years of life lost. Overwhelming evidence demonstrates that reducing LDL-C directly leads to improved cardiovascular outcomes, the clinical risk reduction is linearly-proportional to absolute LDL-C reduction, with each 39 mg/dL reduction in LDL-C yielding a 22% reduction in major coronary events after 12 months of continuous treatment.

Approximately 100 million people worldwide are treated with lipid lowering therapies, predominantly statins, to reduce LDL-C and the associated risk of death, nonfatal myocardial infarction and nonfatal stroke or associated events. Yet cardiovascular disease remains the leading cause of death, highlighting the unmet medical need for additional treatment options for lowering LDL-C. Statins are effective, but are associated with well-known limitations. First, high-intensity oral therapies do not get

all patients to LDL-C goals. This is particularly important in patients with pre-existing coronary heart disease, familial hypercholesterolemia, and/or diabetes, who are at the highest risk and require the most intensive management. Second, not all patients tolerate statins and many are unable to tolerate them at sufficiently high doses. Third, observational studies have demonstrated that >50% of patients do not adhere to oral therapies including statins for more than six months, leaving them completely unprotected against risk of cardiovascular events, including death.

We believe that new long-acting treatment with significant, durable lowering of LDL-C can fulfill important unmet efficacy needs in ASCVD treatment and prevention. Clinical studies performed with inclisiran have demonstrated reductions in LDL-C by more than 50%, when given on top of other lipid lowering therapies, and therefore has the potential to meet this unmet need for additional significant LDL-C reduction. In addition, we believe that inclisiran's twice-a-year dosing administered by a health-care professional aligns with common approaches to care including how often physicians follow up with ASCVD patients. Twice-a-year administration of an LDL-C lowering therapy by a health-care professional can circumvent the challenges of treatment adherence, which has been a significant problem with more frequently dosed therapies and has hampered the ability to make progress against heart disease.

Our Corporate Information

Incorporated in 1996, The Medicines Company's principal executive offices are located at 8 Sylvan Way, Parsippany, New Jersey 07054, and our telephone number is (973) 290-6000. The Medicines Company® name and logo are registered trademarks or trademark applications of The Medicines Company in the United States and/or other countries. All other trademarks, service marks or other tradenames used herein are the property of their respective owners. References to "the Company," "we," "us" or "our" mean The Medicines Company, a Delaware corporation, and its subsidiaries.

The Offering

Common Stock offered by us in this offering	$150,000,000 of shares
Common Stock to be outstanding after this offering	78,173,607 shares (or 78,791,738 shares if the underwriters' option to purchase additional shares is exercised in full) assuming a public offering price of $36.40 per share, the last sale price of our common stock on June 21, 2019.
Option to purchase additional shares offered to the underwriters	The underwriters have an option to purchase up to an additional $22,500,000 of shares of our common stock. The underwriters can exercise this option at any time within 30 days from the date of this prospectus supplement.
Use of proceeds	We estimate that the net proceeds from this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $140.7 million (or approximately $161.9 million if the underwriters exercise in full their option to purchase additional shares), based on an assumed public offering price of $36.40 per share, the last sale price of our common stock on June 21, 2019, as reported on the NASDAQ Global Select Market. We intend to use the net proceeds from the shares sold by us in this offering to fund our development of inclisiran and for general corporate purposes, which may include the acquisition of complementary products, technologies or businesses, pre-commercial activities, repayment and refinancing of debt, working capital and capital expenditures. See "Use of Proceeds."
Risk factors	You should read the "Risk Factors" section of this prospectus supplement beginning on page S-10 for a discussion of factors to consider before deciding to purchase shares of our common stock.
NASDAQ Global Select Market symbol	MDCO

The number of shares of our common stock to be outstanding after this offering is based on 74,052,728 shares outstanding as of June 20, 2019, and excludes:

- 10,656,145 shares of common stock issuable upon the exercise of outstanding stock options as of June 20, 2019 at a weighted-average exercise price of approximately $29.25 per share;
- an aggregate of 16,020,887 additional shares of common stock reserved for future issuance under our stock incentive and employee stock purchase plans as of June 20, 2019; and
- shares of common stock, if any, issuable upon conversion of our 2.50% Convertible Senior Notes due 2022 (the "2022 Notes"), 2.75% Convertible Senior Notes due 2023 (the "2023 Notes") or 3.50% Convertible Senior Notes due 2024 (the "2024 Notes").

Except as otherwise noted, we have presented the information in this prospectus supplement assuming:

- no exercise by the underwriters of the option to purchase additional shares of our common stock in this offering; and
- no exercise of outstanding stock options.

Summary Consolidated Financial Data

The following table summarizes our consolidated financial data. We have derived the following consolidated statements of operations data and consolidated statements of comprehensive (loss) income data for the fiscal years ended December 31, 2018, 2017 and 2016 and the consolidated balance sheet data as of December 31, 2018 and 2017 from our audited consolidated financial statements, incorporated by reference into this offering memorandum. We have derived the consolidated statements of operations data and consolidated statements of comprehensive (loss) income data for the three months ended March 31, 2019 and 2018 and the summary consolidated balance sheet data as of March 31, 2019 from our unaudited consolidated financial statements, incorporated by reference into this offering memorandum. The results of operations for the interim periods are not necessarily indicative of results to be expected for the full year or any future period. The unaudited consolidated financial statements have been prepared on the same basis as the audited consolidated financial statements. Our historical results for any prior period are not necessarily indicative of results to be expected for any future period. You should read the summary consolidated financial data provided.

below in conjunction with our consolidated financial statements and accompanying notes which are incorporated by reference into this offering memorandum.

(In thousands, except per share data)	Three months ended March 31, 2019	Three months ended March 31, 2018	Year Ended December 31, 2018	Year Ended December 31, 2017	Year Ended December 31, 2016
	(Unaudited)				
Consolidated statements of operations data:					
Net revenues	$ —	$ 7,771	$ 6,138	$ 44,789	$ 143,161
Operating expenses:					
Cost of revenues	—	2,737	7,255	47,193	60,653
Asset impairment charges			5,073	392,097	—
Research and development	27,011	40,366	133,007	138,370	92,107
Selling, general and administrative	16,982	28,951	52,214	132,225	212,482
Total operating expenses	43,993	72,054	197,549	709,885	365,242
Loss from operations	(43,993)	(64,283)	(191,411)	(665,096)	(222,081)
Co-promotion and license income	—	228	1,019	7,549	3,854
Loss on short-term investment	(266)	(29,989)	(51,881)	—	—
Gain on sale of business			—	—	288,301
Loss on extinguishment of debt			—	—	(5,380)
Interest expense	(16,024)	(12,077)	(49,411)	(48,564)	(44,463)
Other income	421	2,369	5,580	1,840	346
(Loss) income from continuing operations before income taxes	(59,862)	(103,752)	(286,104)	(704,271)	20,577
Benefit from (provision for) income taxes	(3)	18,916	50,888	96,576	(67)
(Loss) income from continuing operations	(59,865)	(84,836)	(235,216)	(607,695)	20,510
Income (loss) from discontinued operations, net of tax	—	113,985	112,060	(100,678)	(139,682)
Net (loss) income	(59,865)	29,149	(123,156)	(708,373)	(119,172)
Net loss attributable to non-controlling interest	—	—	—	—	54
Net loss attributable to The Medicines Company	$ (59,865)	$ 29,149	$ (123,156)	$ (708,373)	$ (119,118)
Amounts attributable to The Medicines Company:					
(Loss) income from continuing operations	$ (59,865)	$ (84,836)	$ (235,216)	$ (607,695)	$ 20,564
Income (loss) from discontinued operations, net of tax	—	113,985	112,060	(100,678)	(139,682)
Net loss attributable to The Medicines Company	$ (59,865)	$ 29,149	$ (123,156)	$ (708,373)	$ (119,118)
Basic (loss) earnings per common share:					
(Loss) earnings from continuing operations	$ (0.80)	$ (1.15)	$ (3.20)	$ (8.40)	$ 0.29
Earnings (loss) from discontinued operations	—	1.54	1.52	(1.39)	(2.00)
Basic loss per share	$ (0.80)	$ 0.39	$ (1.68)	$ (9.79)	$ (1.71)
Diluted (loss) earnings per common share:					
(Loss) earnings from continuing operations	$ (0.80)	$ (1.15)	$ (3.20)	$ (8.40)	$ 0.28
Earnings (loss) from discontinued operations	—	1.54	1.52	(1.39)	(1.91)
Diluted loss per share	$ (0.80)	$ 0.39	$ (1.68)	$ (9.79)	$ (1.63)
Weighted average number of common shares outstanding:					
Basic	74,463	73,802	73,571	72,356	69,909
Diluted	74,463	73,802	73,571	72,356	73,022

(In thousands, except per share data)	Three months ended March 31, 2019	Three months ended March 31, 2018	Year Ended December 31, 2018	Year Ended December 31, 2017	Year Ended December 31, 2016
	(Unaudited)				
Consolidated statements of comprehensive (loss) income data:					
Net loss	$ (59,865)	$ 29,149	$ (123,156)	$ (708,373)	$ (119,172)
Other comprehensive income (loss):					
Foreign currency translation adjustment	(830)	(471)	(576)	296	213
Amounts reclassified from accumulated other comprehensive income (loss)	—	1,183	1,183	—	(9,665)
Other comprehensive income (loss)	(830)	712	607	296	(9,452)
Comprehensive loss	(60,695)	29,861	(122,549)	(708,077)	(128,624)
Less: comprehensive loss attributable to non-controlling interest	—	—	—	—	54
Comprehensive loss attributable to The Medicines Company	$ (60,695)	$ 29,861	$ (122,549)	$ (708,077)	$ (128,570)

(In thousands)	As of March 31, 2019	As of December 31, 2018	As of December 31, 2017
	(Unaudited)		
Consolidated balance sheet data:			
Cash and cash equivalents, available for sale securities and accrued interest receivable	$ 199,736	$ 238,310	$ 151,359
Working capital	$ 194,954	$ 236,392	$ 387,812
Total assets	$ 835,853	$ 841,686	$ 872,983
Long-term liabilities	$ 848,097	$ 805,539	$ 672,577
Accumulated deficit	$(1,440,589)	$(1,380,724)	$(1,257,356)
Total stockholders' (deficit) equity	$ (75,389)	$ (22,264)	$ 24,914

RISK FACTORS

Investing in our common stock involves a high degree of risk. In deciding whether to invest, you should consider carefully the risks and uncertainties described below, as well as the other information contained in this prospectus supplement, the accompanying prospectus and in our filings with the SEC, that we have incorporated by reference in this prospectus supplement and the accompanying prospectus. Any of the following risks could have a material adverse effect on our business, financial condition, results of operations and prospects and cause the value of our stock to decline, which could cause you to lose all or part of your investment. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Related to Development, Approval and Commercialization of Inclisiran

We are almost entirely dependent on the success of inclisiran, our only drug candidate, which is currently in Phase 3 of clinical development, and we cannot be certain that inclisiran will receive regulatory approval or be successfully commercialized even if we receive regulatory approval.

Following our divestiture of Angiomax in the United States to Sandoz, we no longer market any products and we may never be able to develop inclisiran as a marketable product. We expect that a substantial majority of our efforts and expenditures over the next few years will be devoted to inclisiran.

Accordingly, our future business, including the ability to generate revenue, finance our operations and repay our indebtedness, depends almost entirely on the successful development, regulatory approval and commercialization of inclisiran. We cannot be certain that inclisiran will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drug products are and will remain subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries that each have differing regulations. We are not permitted to market inclisiran in the United States until it receives approval of an NDA from the FDA, or in any foreign countries until they receive the requisite approval from such countries. Obtaining approval of an NDA is an extensive, lengthy, expensive and inherently uncertain process, and the FDA may delay, limit or deny approval of a drug candidate for many reasons, including:

- we may not be able to demonstrate that inclisiran is safe and effective as a treatment for our targeted indications to the satisfaction of the FDA;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA for marketing approval;
- a clinical research organization ("CRO"), that we retain to conduct clinical trials or any other third parties involved in the conduct of trials may take actions outside of our control that materially adversely impact our clinical trials;
- the FDA may not find the data from pre-clinical studies and clinical trials sufficient to demonstrate that the clinical and other benefits of inclisiran outweigh the safety risks;
- the FDA may disagree with our interpretation of data from our pre-clinical studies and clinical trials or may require that we conduct additional studies or trials;
- the FDA may not accept data generated at our clinical trial sites;
- if our NDA is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of

approval, additional pre-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;

- the advisory committee may recommend that the FDA require, as a condition of approval, additional pre-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the FDA may require development of a Risk Evaluation and Mitigation Strategy as a condition to approval;
- the FDA may identify deficiencies in the manufacturing processes or facilities of our third-party manufacturers; or
- the FDA may change its approval policies or adopt new regulations.

If inclisiran gains regulatory approval, the commercial launch will require significant efforts from us. Our ability to successfully commercially launch inclisiran will depend on our ability to:

- train, deploy and support a qualified sales force to market and sell our newly launched product;
- have third parties manufacture and release the product in sufficient quantities;
- implement and maintain agreements with wholesalers and distributors;
- receive adequate levels of coverage and reimbursement for the product from governments and third-party payors;
- develop and execute marketing and sales strategies and programs for the product; and
- enter into suitable partnerships with third parties, as needed, to provide a viable platform to commercialize the product.

We expect that the revenues from inclisiran, if approved, will represent nearly all of our revenues in the future. As a result, if we are unable to successfully commercialize inclisiran, our business, results of operations and financial condition would be materially harmed.

We will need substantial additional funds to support our operations, and amounts we previously expected to be paid to us by Melinta may not be received and additional funding may not be available to us on acceptable terms, or at all.

We are focused on the advancement of our product candidate, inclisiran. The completion of the development and the potential commercialization of inclisiran, should it receive regulatory approval, will require that we obtain substantial additional funds.

Due to the divesture of our rights to branded Angiomax in the United States to Sandoz during the three months ended September 30, 2018, we are no longer generating revenues from product sales. Prior to such divestiture, our revenues generated from product sales had been declining significantly since 2014 due to the introduction of generic competition to Angiomax and the divestiture of certain of our non-core products. We have incurred net losses and negative cash flows from operations since 2014 and had an accumulated deficit of approximately $1.4 billion as of March 31, 2019. We expect to incur significant expenses and operating losses for the foreseeable future as we continue to develop, seek regulatory approval for and potentially commercializes inclisiran.

Melinta has significant payment commitments to us, including a $25 million deferred payment which was due on January 7, 2019 and an additional $25 million deferred payment due July 8, 2019, and quarterly payments based on net sales of Orbactiv and Minocin and, subject to a $50 million annual net sales threshold, Vabomere. In addition, Melinta assumed our obligation to make a $30 million milestone payment to the former owners of the infectious disease business, which we refer

to as the Vabomere Milestone Payment, upon receipt of regulatory approval of Vabomere by the European Medicines Agency, which approval was received by Melinta in November 2018. We remain ultimately responsible to pay the Vabomere Milestone Payment under our agreement with the former owners of the infectious disease business; however we believe that we are responsible for such payment only if the former owners of the infectious disease business are unable to collect from Melinta after exercising due diligence in attempting to collect from Melinta before seeking to collect from us. In December 2018, Melinta filed a complaint in the Court of Chancery of the State of Delaware alleging that we breached certain representations and warranties in the purchase and sale agreement pursuant to which Melinta acquired our infectious disease business. In addition, in March 2019, Fortis, the representative the former owners of the infectious disease business, filed a complaint in the Court of Chancery of the State of Delaware against Melinta and us regarding the non-payment of the Vabomere Milestone Payment. In connection with Melinta's lawsuit, Melinta is seeking indemnification under the purchase and sale agreement and notified us that it would not be paying the Vabomere Milestone Payment or the first of two $25 million deferred payments due to us under the purchase and sale agreement because Melinta believes it has the right to set-off such payments against its claimed damages in its lawsuit. Although we believe Melinta's claims are meritless and we will vigorously defend any and all claims brought against us by Melinta and seek full payment by Melinta of its obligations under the purchase and sale agreement, litigation is subject to inherent uncertainty. See "Legal Proceedings" under the Business section of this prospectus supplement for a description of our litigation related to Melinta.

Following the completion of the offering, we believe that our existing cash and cash equivalents (not including any negative outcomes in our pending litigation matters, and assuming no sale of the Melinta shares of common stock that we own), will be sufficient to satisfy our anticipated operating and other funding requirements for the next twelve months from June 25, 2019 (the date of this prospectus supplement), including the receipt of clinical results from our ongoing Phase III trial of inclisiran and our anticipated submission of an NDA with the FDA and a European Marketing Authorization with the EU.

If we are unable to successfully develop our business infrastructure and operations, our ability to generate future product revenue will be adversely affected and our business, results of operations and financial condition may be adversely affected.

We need to properly scale our internal organization and infrastructure to accommodate the development and, upon approval, commercialization of inclisiran. To manage our future growth and the breadth and complexity of our activities, we need to properly invest in personnel, infrastructure, information management systems and other operational resources. If we are unable to scale global operations successfully and in a timely manner, the growth of our business may be limited. Developing our business infrastructure and operations may be more difficult, more expensive or take longer than we anticipate.

Future development of our business infrastructure and operations could strain our operational, human and financial resources. In order to manage the development of our business infrastructure and global operations, we must:

- continue to improve operating, administrative, and information systems;
- accurately predict future personnel and resource needs to meet contract commitments;
- track the progress of ongoing projects; and
- attract and retain qualified management, sales, professional, scientific and technical operating personnel.

If we do not take these actions and are not able to manage our business, then our operations may be less successful than anticipated.

Risks Related to Our Financial Results

We have a history of net losses and may not achieve profitability in future periods.

We have incurred net losses in many years and on a cumulative basis since our inception, and we expect to continue to incur net losses.

As of March 31, 2019, we had an accumulated deficit of approximately $1.4 billion. In those periods in which we were able to achieve profitability, our profitability was based on revenue from sales of Angiomax, and a substantial majority of our historic revenue has been generated from sales of Angiomax in the United States. However, in August 2018 we divested Angiomax in the United States to Sandoz following a period of generic competition for Angiomax that commenced in the United States in July 2015 and in Europe in August 2015.

We expect to make substantial expenditures to further develop and commercialize inclisiran, including costs and expenses associated with research and development, clinical trials, nonclinical and preclinical studies, regulatory approvals and commercialization. We will need to generate significant revenue in future periods from inclisiran in order to achieve and maintain profitability. If we are unable to generate significant revenue, we may not achieve profitability in future periods. Our ability to generate future revenue will be substantially dependent on our ability to successfully commercialize inclisiran. If we fail to achieve profitability within the time frame expected by investors or securities analysts, the market price of our common stock may decline.

We need to raise additional capital. If we are unable to obtain such capital on favorable terms or at all, we will not be able to execute on our business plans and our business, financial condition and results of operations will be adversely affected.

At March 31, 2019, we had approximately $199.7 million in cash and cash equivalents. We expect to devote substantial financial resources to our research and development efforts, clinical trials, nonclinical and preclinical studies and regulatory approvals and to our commercialization and manufacturing programs associated with inclisiran. We also will require cash to pay interest on the $172.5 million aggregate principal amount of 2024 Notes, the $400.0 million aggregate principal amount of the 2022 Notes and the $402.5 million aggregate principal amount of the 2023 Notes, and to make principal payments on the 2024 Notes, the 2022 Notes and 2023 Notes at maturity or upon conversion (other than the 2023 and 2024 Notes upon conversion, in which case we will have the option to settle entirely in shares of our common stock).

In addition, as of June 21, 2019, our total potential milestone payment obligations related to development, regulatory and commercial milestones for inclisiran, assuming all milestones are achieved in accordance with the terms of our license and collaboration agreement with Alnylam, would be $150.0 million. Of this amount, $50.0 million relates to regulatory approval milestones and $100.0 million relates to commercial milestones. We had additional contingent cash payments relating to pre-clinical infectious disease assets acquired in our Rempex acquisition (and which were not divested in the Melinta transactions), but the obligations for such payments were assumed by Qpex in its acquisition of the pre-clinical infectious disease assets in October 2018. In addition, even though Melinta assumed our obligation to make the Vabomere Milestone Payment, we remain ultimately responsible to pay the Vabomere Milestone Payment under our agreement with the former owners of the infectious disease business; however we believe that we are responsible for such payment only if the former owners of the infectious disease business are unable to collect from Melinta after exercising due diligence in attempting to collect from Melinta before seeking to collect from us. See "Legal

Proceedings" under the Business section of this prospectus supplement for a description of our litigation related to Melinta.

In addition, of the total potential milestone payment obligations, based on our anticipated timeline for the achievement of development, regulatory and commercial milestones, we do not expect that we would make milestone payments under our license agreement and collaboration agreement with Alnylam during 2019. We continually evaluate our liquidity requirements, capital needs and availability of resources in view of, among other things, alternative sources and uses of capital, debt service requirements, the cost of debt and equity capital and estimated future operating cash flow. We may raise additional capital; generate cash proceeds from entering into collaboration agreements with respect to inclisiran; restructure or refinance outstanding debt; repurchase material amounts of outstanding debt or equity; or take a combination of such steps or other steps to increase or manage our liquidity and capital resources. Any such actions or steps could have a material effect on us.

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

- the progress, level, timing and cost of our research and development activities related to our clinical trials and non-clinical studies with respect to inclisiran;
- whether we develop and commercialize inclisiran on our own or through licenses and collaborations with third parties and the terms and timing of such arrangements, if any;
- the extent to which our submissions and planned submissions for regulatory approval of inclisiran are approved on a timely basis, if at all;
- if inclisiran receives regulatory approval, the extent to which it is commercially successful;
- the extent to which we are able to realize additional funds through our sources of liquidity from the Melinta transaction or from the future payments, if any, which we are entitled from Melinta due to the sale of the infectious disease business and connected to our ongoing litigation with Melinta;
- the continuation or termination of third-party manufacturing, distribution and sales and marketing arrangements;
- the size, cost and effectiveness of our sales and marketing programs, including scaling our operations in anticipation of a potential launch of inclisiran;
- the amounts of our payment obligations to third parties with respect to inclisiran;
- our ability to defend and enforce our intellectual property rights; and
- our ability to defend ourselves and prevail in current and, if any, future litigation matters.

With respect to both our short-term and long-term cash requirements, if our existing cash resources, together with cash that we generate from sales of our products and other sources, are insufficient to satisfy our research and development, clinical trial, product commercialization and other funding requirements, including obligations under our convertible notes, we will need to sell additional equity or debt securities, engage in asset sales, engage in other strategic transactions, or seek additional financing through other arrangements, any of which could be material. Any sale of additional equity or convertible debt securities may result in dilution to our stockholders. Public or private financing may not be available in amounts or on terms acceptable to us, if at all. If we seek to raise funds through collaboration or licensing arrangements with third parties, we may be required to relinquish rights to products, products in development or technologies that we would not otherwise relinquish or grant licenses on terms that may not be favorable to us. Moreover, our ability to obtain additional debt financing may be limited by the 2024 Notes, the 2022 Notes and the 2023 Notes, market conditions or otherwise. If we are unable to obtain additional financing or otherwise increase our cash resources, we

may be required to delay, reduce the scope of, or eliminate one or more of our planned research, development and commercialization activities, which could adversely affect our business, financial condition and operating results.

If we seek to raise additional capital by selling equity or debt securities or through other arrangements in the future, our stockholders could be subject to dilution and we may become subject to financial restrictions and covenants, which may limit our activities.

If we determine that raising capital would be in the interest of the company and our stockholders, we may seek to sell equity or debt securities or seek financing through other arrangements. Any sale of equity or debt securities may result in dilution to our stockholders and increased liquidity requirements. Debt financing may involve covenants limiting or restricting our ability to take specific actions, such as incurring additional debt or making capital expenditures. Our ability to comply with these financial restrictions and covenants could be dependent on our future performance, which is subject to prevailing economic conditions and other factors, including factors that are beyond our control such as foreign exchange rates, interest rates and changes in the level of competition. Failure to comply with the financial restrictions and covenants would adversely affect our business, financial condition and operating results.

We have been subject to securities class action litigation and may be subject to similar or other litigation in the future, which may divert management's attention and have a material adverse effect on our business, financial condition and results of operations.

In February 2014, a class action lawsuit was filed against us and certain of our current and former officers alleging, among other things, that we and certain of our current and former officers violated federal securities laws because we and certain current and former officers allegedly made misrepresentations or did not make proper disclosures regarding the results of clinical trials which tested the efficacy and safety of one of our recently divested products. On February 12, 2016, the parties executed a stipulation for a proposed class settlement, subject to court approval, and on June 7, 2016, the court granted final approval of the settlement.

There may be additional suits or proceedings brought in the future. Monitoring and defending against legal actions, whether or not meritorious, is time-consuming for our management and detracts from our ability to fully focus our internal resources on our business activities, and we cannot predict how long it may take to resolve these matters. In addition, we may incur substantial legal fees and costs in connection with litigation. Although we have insurance, coverage could be denied or prove to be insufficient.

We may be limited in our ability to utilize, or may not be able to utilize, deferred tax assets to reduce our future tax liability.

We are subject to income taxes in the United States and numerous foreign jurisdictions. The amount of income taxes we owe is subject to the application of tax laws in jurisdictions in which we file. Changes in current or future laws or regulations, the imposition of new or changed tax laws or regulations or new related interpretations by taxing authorities in the jurisdictions in which we file could materially adversely affect our financial condition, results of operations, and cash flows.

Our future income tax liability may be significantly reduced by tax credits and net operating loss carryforwards available to us under the applicable tax codes. However, utilization of these net operating loss and tax credit carryforwards is dependent upon the Company achieving profitable results. At December 31, 2018, we had a valuation allowance that fully offset our net deferred tax assets.

If a corporation experiences an "ownership change," Sections 382 and 383 of the Code (as defined herein) provide annual limitations with respect to the ability of the corporation to utilize its net

operating loss (as well as certain built-in losses) and tax credit carryforwards against future U.S. taxable income. In general, an ownership change may result from transactions increasing the ownership of certain stockholders in the stock of the corporation by more than 50 percentage points over a three-year testing period. Certain of our tax attributes are subject to limitations as a result of historic ownership changes. Our use of net operating loss and tax credit carryforwards may be further limited by Section 382 of the Code as a result of any future ownership changes. In this event, the Company could owe significantly more tax, and could owe tax sooner than it would if it was able to fully use its net operating loss.

Risks Related to Our Notes

We have incurred substantial indebtedness, and our leverage and maintenance of high levels of indebtedness may adversely affect our business, financial condition and results of operations. Servicing this debt, including the 2022 Notes, the 2023 Notes and the 2024 Notes, will require a significant amount of cash, and we may not have sufficient cash flow from our business to pay the interest on or principal of the 2022 Notes, the 2023 Notes, the 2024 Notes or other debt we may incur.

We have incurred a significant amount of indebtedness and may incur additional indebtedness in the future. Our maintenance of this level of indebtedness could have adverse consequences, including:

- requiring us to dedicate a substantial portion of cash flow from operations to the payment of interest on, and principal of, our debt, which will reduce the amounts available to fund working capital, capital expenditures, product development efforts and other general corporate purposes;
- increasing our vulnerability to general adverse economic, industry and market conditions;
- limiting our ability to obtain additional financing in the future or engage in certain strategic transactions without securing bondholder consent;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a possible competitive disadvantage to less leveraged competitors and competitors that have less debt, better debt servicing options or better access to capital resources.

In addition, our ability to make scheduled payments of the principal of, to pay interest on or to refinance the remaining amount outstanding under the 2022 Notes, the 2023 Notes or the 2024 Notes depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations in the future sufficient to service our debt, including the notes. If we are unable to generate cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be unfavorable to us or highly dilutive, any of which may be material to the holders of our common stock. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at the time we seek to refinance such indebtedness. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

We may not have the ability to raise the funds necessary to settle conversions of the 2022 Notes or to repurchase the 2022 Notes, the 2023 Notes or 2024 Notes upon a fundamental change, and our future debt may contain limitations on our ability to pay cash upon conversion of the 2022 Notes or repurchase of the 2022 Notes, 2023 Notes or 2024 Notes.

Holders of the 2022 Notes, the 2023 Notes and the 2024 Notes will have the right to require us to repurchase their notes upon the occurrence of a fundamental change, as defined in the applicable indenture, at a repurchase price equal to 100% of their principal amount, plus accrued and unpaid

interest, if any, as described in the applicable indenture. In addition, upon conversion of the 2022 Notes, we will be required to make with respect to each $1,000 in principal amount of notes converted cash payments of at least the lesser of $1,000 and the sum of the daily conversion values as described in the applicable indenture. Upon conversion of the 2023 Notes and the 2024 Notes, we will have the option to settle such conversions in cash, shares of our common stock or a combination thereof. However, we may not have enough available cash or be able to obtain financing at the time we are required to repurchase notes, to pay the notes at maturity or to pay cash upon conversions of such notes. In addition, our ability to repurchase notes or to pay cash upon conversions of such notes may be limited by law, by regulatory authority or by agreements governing our existing indebtedness (including, in the case of the 2022 Notes, the 2023 Notes or the 2024 Notes, the indenture governing any other series of notes) and future indebtedness. Our failure to repurchase notes at a time when the repurchase is required by the applicable indenture or to pay any cash payable on future conversions of the notes as required by the applicable indenture would constitute a default under the applicable indenture. A default under the applicable indenture governing the 2022 Notes, the 2023 Notes or 2024 Notes, or the fundamental change itself could also lead to a default under agreements governing our existing indebtedness (including, in the case of the 2022 Notes, the 2023 Notes or 2024 Notes, the indenture governing any other series of notes) and future indebtedness. If the repayment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and repurchase the notes or make cash payments upon conversions thereof.

The conditional conversion feature of the 2022 Notes, the 2023 Notes or the 2024 Notes, if triggered, may adversely affect our financial condition and operating results.

In the event the conditional conversion feature of the 2022 Notes, the 2023 Notes or the 2024 Notes is triggered, holders of such notes will be entitled to convert the notes at any time during specified periods at their option, which are set forth in the applicable indenture. If one or more holders elect to convert their 2022 Notes, we would be required, with respect to each $1,000 principal amount of 2022 Notes, to make cash payments equal to the lesser of $1,000 and the sum of the daily conversion values, which could adversely affect our liquidity. If the holders of all of the 2022 Notes were able to exercise their conversion option, we would not have sufficient cash to satisfy our payment obligations with respect to all of the 2022 Notes and meet our anticipated funding requirements for a year from June 25, 2019 (the date of this prospectus supplement). With respect to the 2023 Notes and 2024 Notes, we have the option to settle conversions entirely in cash, in common stock or a combination thereof. In addition, even if holders do not elect to convert their notes, we are required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the notes as a current rather than long-term liability, which results in a material reduction of our net working capital.

The accounting method for convertible debt securities that may be settled in cash, such as the 2022 Notes, the 2023 Notes and 2024 Notes, could have a material effect on our reported financial results.

Under Accounting Standards Codification 470-20, "Debt with Conversion and Other Options", which we refer to as ASC 470-20, an entity must separately account for the liability and equity components of the convertible debt instruments that may be settled entirely or partially in cash upon conversion (such as the 2022 Notes, the 2023 Notes and the 2024 Notes) in a manner that reflects the issuer's economic interest cost. The effect of ASC 470-20 on the accounting for the 2022 Notes, the 2023 Notes and the 2024 Notes is that the equity component is required to be included in the additional paid in capital section of stockholders' equity on our consolidated balance sheet, and the value of the equity component would be treated as original issue discount for purposes of accounting for the debt component of the 2022 Notes, the 2023 Notes and the 2024 Notes. As a result, we will be required to record a greater amount of non-cash interest expense in current periods presented as a

result of the amortization of the discounted carrying value of the notes to their face amount over the term of the 2022 Notes, the 2023 Notes and the 2024 Notes. We will report lower net income in our financial results because ASC 470-20 will require interest to include both the current period's amortization of the debt discount and the instrument's coupon interest, which could adversely affect our reported or future financial results, the market price of our common stock and the trading price of the 2022 Notes, the 2023 Notes and the 2024 Notes.

In addition, under certain circumstances, convertible debt instruments that may be settled entirely or partly in cash (such as the 2022 Notes) are currently accounted for utilizing the treasury stock method, the effect of which is that the shares issuable upon conversion of the notes are not included in the calculation of diluted earnings per share except to the extent that the conversion value of the notes exceeds their principal amount. Under the treasury stock method, for diluted earnings per share purposes, the transaction is accounted for as if the number of shares of common stock that would be necessary to settle such excess are issued. We cannot be sure that the accounting standards in the future will continue to permit the use of the treasury stock method. If we are unable to use the treasury stock method in accounting for the shares issuable upon conversion of the 2022 Notes, then our diluted earnings per share would be adversely affected.

Additional Risks Related to Commercialization

We face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.

Our industry is highly competitive. Competitors in the United States and other countries include major pharmaceutical companies, specialty pharmaceutical companies and biotechnology firms, universities and other research institutions. Many of our competitors are substantially larger than we are and have substantially greater research and development capabilities and experience, and greater manufacturing, marketing and financial resources, than we do.

Our competitors may develop, market or license products or novel technologies that are more effective, safer, more convenient or less costly than any that are being developed by us, or may obtain marketing approval for their products from the FDA or equivalent foreign regulatory bodies more rapidly than we may obtain approval for ours. There are well established products, including in many cases generic products, that are approved and marketed for the indications for which we are developing inclisiran. In addition, competitors are developing products for such markets and indications. A description of the competition for inclisiran is included in "Business—Competition" below.

We expect inclisiran to compete on the basis of product efficacy, safety, ease of administration, price and economic value compared to drugs used in current practice or currently being developed. If we are not successful in demonstrating these attributes, physicians and other key healthcare decision makers may choose other products over our products, switch from our products to new products or choose to use our products only in limited circumstances, which could adversely affect our business, financial condition and results of operations.

If reimbursement by government payers or other third-party payers is not available or limited for our products, pricing is delayed or set at unfavorable levels or access to our products is reduced or terminated by governmental and other third-party payers, our ability to generate revenue would be adversely affected.

Acceptable levels of coverage and reimbursement of drug treatments by government payers, such as Medicare and Medicaid programs, private health insurers and other organizations, have a significant effect on our ability to successfully commercialize our products. Reimbursement in the United States, Europe or elsewhere may not be available for any products we may develop or, if already available, may be decreased in the future. We may not get reimbursement or reimbursement may be limited if government payers, private health insurers and other organizations are influenced by the prices of

existing drugs in determining whether our products will be reimbursed and at what levels. If reimbursement is not available or is available only at limited levels, we may not be able to commercialize our products, or may not be able to obtain a satisfactory financial return on our products.

In certain countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals and the level of reimbursement are subject to governmental control. In some countries, pricing and reimbursement are set with limited, if any, participation in the process by the marketing authorization holder. In addition, it can take an extended period of time after the receipt of initial approval of a product to establish and obtain reimbursement or pricing approval. Reimbursement approval also may be required at the individual patient level, which can lead to further delays. In addition, in some countries, it may take an extended period of time to collect payment even after reimbursement has been established. If prices are set at unsatisfactory levels, such prices may negatively impact our revenues from sales in those countries. An increasing number of countries are taking initiatives to attempt to reduce large budget deficits by focusing cost-cutting efforts on pharmaceuticals for their state-run health care systems. These international price control efforts have impacted all regions of the world, but have been most drastic in the European Union. Further, a number of European Union countries use drug prices from other countries of the European Union as "reference prices" to help determine pricing in their own countries. Consequently, a downward trend in drug prices for some countries could contribute to similar occurrences elsewhere. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

Third-party payers, including Medicare and Medicaid, increasingly are challenging prices charged for and the cost-effectiveness of medical products and services and they increasingly are limiting both coverage and the level of reimbursement for drugs. If these third-party payers do not consider our products to be economically beneficial compared to other available therapies, they may not cover our products after approval 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 at a profit. Third-party payers may provide coverage, but place stringent limitations on such coverage, such as requiring alternative treatments to be tried first. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. There exists a broader trend in health care in which the government and other payors are seeking to move from individualized "fee for service" payments toward a system focused on "bundled" payments for more comprehensive packages of services and episodes of care. Also, the trend toward managed health care in the United States and the changes in health insurance programs may result in lower prices for pharmaceutical products and health care reform.

Health care reform measures such as those outlined above, and others consistent with these trends, could, among other things, increase pressure on pricing. Additionally, health care reform efforts undertaken during the Trump administration may result in additional reductions in Medicare, Medicaid and other healthcare funding. In addition to federal legislation, state legislatures and foreign governments have also shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. The establishment of limitations on patient access to our drugs, adoption of price controls and cost-containment measures in new jurisdictions or programs, and adoption of more restrictive policies in jurisdictions with existing controls and measures could adversely impact our business and future results. If governmental organizations and third-party payers do not consider our products to be cost-effective compared to other available therapies, they may not reimburse providers or consumers of our products or, if they do, the level of reimbursement may not be sufficient to allow us to sell our products on a profitable basis.

Use or misuse of our products may result in serious injuries or even death to patients and may subject us to significant claims for product liability. If we are unable to obtain insurance at acceptable costs and adequate levels or otherwise protect ourselves against potential product liability claims, we could be exposed to significant liability.

Our business exposes us to potential significant product liability risks which are inherent in the testing, manufacturing, marketing and sale of human healthcare products. Product liability claims might be made by patients in clinical trials, consumers, health care providers or pharmaceutical companies or others that sell our products. These claims may be made even with respect to those products that are manufactured in licensed and regulated facilities or otherwise possess regulatory approval for commercial sale or study.

These claims could expose us to significant liabilities that could prevent or interfere with the development or commercialization of our products. Product liability claims could require us to spend significant time and money in litigation or pay significant damages. With respect to our commercial sales and our clinical trials, we are covered by product liability insurance in the amount of $20.0 million per occurrence and $20.0 million annually in the aggregate on a claims-made basis. This coverage may not be adequate to cover all or any product liability claims that we face.

As we continue to develop inclisiran, we may wish to increase our product liability insurance. Product liability coverage is expensive. In the future, we may not be able to maintain or obtain such product liability insurance on reasonable terms, at a reasonable cost or in sufficient amounts to protect us against losses due to product liability claims.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel and consultants.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on our ability to attract and retain qualified personnel for the acquisition, development and commercialization activities we conduct or sponsor. If we lose one or more of the members of our senior management or other key employees or consultants, our ability to implement successfully our business strategy could be seriously harmed. Our ability to replace these key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to acquire, develop and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate such additional personnel.

Risks Related to our Dependence on Third Parties for Manufacturing, Research and Development, and Distribution Activities

We do not have manufacturing or supply capabilities and are completely dependent on third parties for the manufacture and supply of inclisiran. We depend on a limited number of suppliers for the production of bulk drug substance for inclisiran and to carry out fill-finish activities. If any of these suppliers does not or cannot fulfill its manufacturing or supply obligations to us, our ability to conduct clinical trials of inclisiran could be impaired and our business could be harmed.

We do not manufacture inclisiran and do not plan to develop any capacity to manufacture it. We currently rely on a limited number of manufacturers and other third parties for bulk substance and to carry out fill-finish activities for inclisiran. We expect to continue this manufacturing strategy for the foreseeable future.

In the event that any third-party is unable or unwilling to carry out its respective manufacturing or supply obligations or terminates or refuses to renew its arrangements with us, we may be unable to

obtain alternative manufacturing or supply on commercially reasonable terms on a timely basis or at all. In such cases, the third-party manufacturers have made no commitment to supply the drug product to us on a long-term basis and could reject our purchase orders. Only a limited number of manufacturers are capable of manufacturing inclisiran. Consolidation within the pharmaceutical manufacturing industry could further reduce the number of manufacturers capable of producing our products, or otherwise affect our existing contractual relationships.

If we were required to transfer manufacturing processes to other third-party manufacturers and we were able to identify an alternative manufacturer, we would still need to satisfy various regulatory requirements. Satisfaction of these requirements could cause us to experience significant delays in receiving an adequate supply of inclisiran and could be costly. Moreover, we may not be able to transfer processes that are proprietary to the manufacturer. Any delays in the manufacturing process may adversely impact our ability to supply product for clinical trials of inclisiran, which could affect our ability to complete clinical trials of inclisiran on a timely basis and our ability to meet commercial demand for inclisiran, if approved, on a timely basis.

If third parties on whom we rely to manufacture and support the development and commercialization of inclisiran do not fulfill their obligations or we are unable to establish or maintain such arrangements, the development and commercialization of our products may be terminated or delayed, and the costs of development and commercialization may increase.

Our development and commercialization strategy involves entering into arrangements with corporate and academic collaborators, contract research organizations, distributors, third-party manufacturers, licensors, licensees and others to conduct development work, manage or conduct our clinical trials, manufacture our products and market and sell our products outside of the United States. We do not have the expertise or the resources to conduct many of these activities on our own and, as a result, are particularly dependent on third parties in many areas.

We may not be able to establish and maintain arrangements to develop, manufacture and, if approved, commercialize inclisiran or any additional product candidates or products we may acquire on terms that are acceptable to us. Any current or future arrangements for development and commercialization may not be successful. If we are not able to establish or maintain agreements relating to inclisiran or any additional products or product candidates we may acquire, our results of operations would be materially adversely affected.

Third parties may not perform their obligations as expected. The amount and timing of resources that third parties devote to developing, manufacturing and commercializing our products are not within our control. Our collaborators may develop, manufacture or commercialize, either alone or with others, products and services that are similar to or competitive with the products that are the subject of the collaboration with us. Furthermore, our interests may differ from those of third parties that manufacture or commercialize our products. Our collaborators may reevaluate their priorities from time to time, including following mergers and consolidations, and change the focus of their development, manufacturing or commercialization efforts. Disagreements that may arise with these third parties could delay or lead to the termination of the development or commercialization of our product candidates, or result in litigation or arbitration, which would be time consuming and expensive.

If any third party that manufactures or supports the development or commercialization of our products breaches or terminates its agreement with us, fails to commit sufficient resources to our

collaboration or conduct its activities in a timely manner, or fails to comply with regulatory requirements, such breach, termination or failure could:

- delay or otherwise adversely impact the manufacturing, development or commercialization of inclisiran or any additional products or product candidates that we may acquire or develop;
- require us to seek a new collaborator or undertake unforeseen additional responsibilities or devote unforeseen additional resources to the manufacturing, development or commercialization of our products; or
- result in the termination of the development or commercialization of our products.

Our reliance on third-party manufacturers and suppliers to supply inclisiran may increase the risk that we will not have appropriate supplies of the product or that sanctions may be imposed on us or the manufacturer due to a manufacturer's failure to comply with regulation requirements, either of which could adversely affect our business, results of operations and financial condition.

Reliance on third-party manufacturers and suppliers entails risks to which we would not be subject if we manufactured inclisiran ourselves, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing or supply agreement by the third party; and
- the possible termination or non-renewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us.

Inclisiran may compete with products of third parties for access to manufacturing facilities. If we are not able to obtain adequate supplies of our products, it will be more difficult for us to compete effectively and develop inclisiran.

Our manufacturers are subject to ongoing, periodic, unannounced inspection by the FDA and corresponding state and foreign agencies or their designees to evaluate compliance with the FDA's current good manufacturing practices ("cGMP"), regulations and other governmental regulations and corresponding foreign standards. We cannot be certain that our present or future manufacturers will be able to comply with cGMP regulations and other FDA regulatory requirements or similar regulatory requirements outside the United States. We do not control compliance by our manufacturers with these regulations and standards. Failure of our third-party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on the manufacturer or us, including fines and other monetary penalties, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our products in development, delays, suspension or withdrawal of approvals, suspension of clinical trials, license revocation, seizures or recalls of products in development or products, interruption of production, warning letters, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of inclisiran.

We may depend on collaborations with third parties for the development and commercialization of inclisiran. If those collaborations, if entered into, are not successful, we may not be able to capitalize on the market potential of inclisiran.

We may seek to develop and commercialize inclisiran through a variety of types of collaboration arrangements. Our likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We may not be able to enter into

these types of arrangements on a timely basis, on favorable terms or at all. Our ability to enter into such arrangements with respect to inclisiran that are subject to licenses may be limited by the terms of those licenses. If we do enter into any such arrangements with any third parties in the future, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of inclisiran. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving inclisiran could pose a number of risks to us, including:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of inclisiran or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon inclisiran, repeat or conduct new clinical trials or require a new formulation of inclisiran for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products in development if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or otherwise expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or products in development or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable products and products in development.

Collaboration agreements may not lead to development or commercialization of products in development in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

If we use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages or subject to fines and penalties.

Prior to our divestiture of our pre-clinical infectious disease assets to Qpex, we conducted research and development activities that involved the controlled use of potentially hazardous substances, including chemical, biological and radioactive materials and viruses. In addition, our operations produced hazardous waste products. Federal, state and local laws and regulations in the United States and Canada govern the use, manufacture, storage, handling and disposal of hazardous materials. With respect to research and development activities conducted prior to our divestiture of our pre-clinical infectious disease assets, we may incur liability as a result of contamination or injury resulting from hazardous materials, which could exceed our resources. We have only limited insurance for liabilities arising from hazardous materials.

Additional Risks Related to Regulatory Matters

Clinical trials of product candidates are expensive and time-consuming, and the results of these trials are uncertain. If we are unable to conduct clinical trials that continue to demonstrate the safety and efficacy of inclisiran on a timely basis, then our costs of developing inclisiran may increase and we may not be able to obtain regulatory approval for inclisiran on a timely basis or at all.

Before we can obtain regulatory approvals to market inclisiran, we will be required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of such product for such indication.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. Success in pre-clinical testing or early clinical trials does not ensure that later clinical trials will be successful, and interim results of a clinical trial do not necessarily predict final results. An unexpected result in one or more of our clinical trials can occur at any stage of testing. For example, in November 2016, we voluntarily discontinued our clinical development program for MDCO-216, an investigational cholesterol efflux promoter, and in August 2017 we voluntarily discontinued our clinical development program for MDCO-700, an investigational anesthetic agent.

We may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent us from receiving regulatory approval or commercializing our inclisiran, including:

- our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials which even if undertaken cannot ensure we will gain approval;
- data obtained from pre-clinical testing and clinical trials may be subject to varying interpretations, which could result in the FDA or other regulatory authorities deciding not to approve a product in a timely fashion, or at all;
- the cost of clinical trials may be greater than we currently anticipate;
- regulators, ethics committees or institutional review boards may not authorize us to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we, or the FDA or other regulatory authorities, might suspend or terminate a clinical trial at any time on various grounds, including a finding that participating patients are being exposed to unacceptable health risks. For example, we have in the past voluntarily suspended enrollment in one of our clinical trials to review an interim analysis of safety data from the trial; and

- the effects of inclisiran may not be the desired effects or may include undesirable side effects or inclisiran may have other unexpected characteristics.

The rate of completion of clinical trials depends in part upon the rate of enrollment of patients. Patient enrollment is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the existence of competing clinical trials and the availability of alternative or new treatments. Delays in patient enrollment in any of our current or future clinical trials may result in increased costs and program delays.

If we or the contract manufacturers manufacturing inclisiran fail to comply with the extensive regulatory requirements to which we, our contract manufacturers and inclisiran are subject, the development of inclisiran could be jeopardized and we could be subject to penalties.

The research, testing, manufacturing, labeling, safety, advertising, promotion, storage, sales, distribution, import, export and marketing, among other things, of our products, both before and after approval, are subject to extensive regulation by governmental authorities in the United States, Europe and elsewhere throughout the world. Both before and after approval of a product, quality control and manufacturing procedures must conform to cGMP. Regulatory authorities, including the FDA, periodically inspect manufacturing facilities to assess compliance with cGMP. Our failure or the failure of contract manufacturers to comply with the laws administered by the FDA, the EMA or other governmental authorities could result in, among other things, any of the following:

- delay in approving or refusal to approve a product;
- product recall or seizure;
- suspension or withdrawal of an approved product from the market;
- delays in, suspension of or prohibition of commencing, clinical trials of inclisiran;
- interruption of production;
- operating restrictions;
- untitled or warning letters;
- injunctions;
- fines and other monetary penalties;
- the imposition of civil or criminal penalties;
- disruption of importing and exporting activities; and
- unanticipated expenditures.

We may incur significant liability if it is determined that we are engaging in pre-approval promotion or, if approved, promoting the "off-label" use of inclisiran.

Physicians may prescribe drug products for uses that are not described in the product's labeling and that differ from those approved by the FDA or other applicable regulatory agencies. Off-label uses are common across medical specialties. Although the FDA and other regulatory agencies do not regulate a physician's choice of treatments, the FDA and other regulatory agencies do restrict communications on the subject of off-label use. Companies may not promote drugs for off-label uses. In addition, the FDA prohibits the promotion of drugs that have not yet been approved or cleared for

any use. The FDA and other regulatory and enforcement authorities actively enforce laws and regulations prohibiting promotion of off-label uses and products for which marketing approval has not been obtained. A company that is found to have engaged in pre-approval promotion and promoted off-label uses may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions.

Notwithstanding the regulatory restrictions on pre-approval promotion and off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific exchange concerning their products. We engage in medical education activities and communicate with investigators and potential investigators regarding our clinical trials. If the FDA or another regulatory or enforcement authority determines that our communications regarding inclisiran are not in compliance with the relevant regulatory requirements, we may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions.

If we do not comply with federal, state and foreign laws and regulations relating to the health care business, we could face substantial penalties.

We and our customers are subject to extensive regulation by the federal government, and the governments of the states and foreign countries in which we may conduct our business. In the United States, the laws that directly or indirectly affect our ability to operate our business include the following:

- the Federal Anti-Kickback Law, which prohibits persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce either the referral of an individual or furnishing or arranging for a good or service for which payment may be made under federal health care programs such as Medicare and Medicaid;

- other Medicare laws and regulations that prescribe the requirements for coverage and payment for services performed by our customers, including the amount of such payment;

- the Federal False Claims Act, which imposes civil and criminal liability on individuals and entities who submit, or cause to be submitted, false or fraudulent claims for payment to the government;

- the Federal False Statements Act, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with delivery of or payment for health care benefits, items or services; and

- various state laws that impose similar requirements and liability with respect to state healthcare reimbursement and other programs.

If our operations are found to be in violation of any of the laws and regulations described above or any other law or governmental regulation to which we or our customers are or will be subject, we may be subject to civil and criminal penalties, damages, fines, exclusion from the Medicare and Medicaid programs and the curtailment or restructuring of our operations. Similarly, if our customers are found to be non-compliant with applicable laws, they may be subject to sanctions, which could also have a negative impact on us. Any penalties, damages, fines, curtailment or restructuring of our operations would adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses, divert our management's attention from the operation of our business and damage our reputation.

Failure to comply with the U.S. Foreign Corrupt Practices Act ("FCPA"), as well as the anti-bribery laws of the nations in which we conduct business, could subject us to penalties and other adverse consequences.

We are subject to the FCPA, which generally prohibits U.S. companies from engaging in bribery or other prohibited payments to foreign officials for the purpose of obtaining or retaining business and requires companies to maintain accurate books and records and internal controls, including at foreign-controlled subsidiaries. In addition, we are subject to other anti-bribery laws of the nations in which we conduct business that apply similar prohibitions as the FCPA. Our employees or other agents may engage in prohibited conduct without our knowledge under our policies and procedures and the FCPA and other anti-bribery laws that we may be subject to for which we may be held responsible. If our employees or other agents are found to have engaged in such practices, we could suffer severe penalties and other consequences that may have a material adverse effect on our business, financial condition and results of operations.

Risks Related to Our Intellectual Property

If we breach any of the agreements under which we license rights to products or technology from others, we could lose license rights that are material to our business or be subject to claims by our licensors.

We license rights to products and technology that are important to our business, and we expect to enter into additional licenses in the future. For instance, we have exclusively licensed patents and patent applications from Alnylam covering RNAi therapeutics. Under our agreement with Alnylam, we are subject to a range of commercialization and development, sublicensing, royalty, patent prosecution and maintenance, insurance and other obligations.

Any failure by us to comply with any of these obligations or any other breach by us of our license agreements could give the licensor the right to terminate the license in whole, terminate the exclusive nature of the license or bring a claim against us for damages. Any such termination or claim could have a material adverse effect on our financial condition, results of operations, liquidity or business. Even if we contest any such termination or claim and are ultimately successful, such dispute could lead to delays in the development or commercialization of potential products and result in time-consuming and expensive litigation or arbitration. In addition, on termination we may be required to license to the licensor any related intellectual property that we developed.

If we are unable to obtain or maintain protection for the intellectual property relating to our products, the value of our products will be adversely affected.

The patent positions of pharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual issues. We cannot be certain that our patents and patent applications, including our own and those that we have rights to through licenses from third parties, will adequately protect our intellectual property and value of our products. Our success protecting our intellectual property depends significantly on our ability to:

- obtain and maintain U.S. and foreign patents, including defending those patents against adverse claims;
- secure patent term extension for the patents covering our approved products;
- protect trade secrets;
- operate without infringing the proprietary rights of others; and
- prevent others from infringing our proprietary rights.

We may not have any additional patents issued from any patent applications that we own or license. If additional patents are granted, the claims allowed may not be sufficiently broad to protect

our technology. In addition, issued patents that we own or license may be challenged in contested proceedings such as opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings and may be narrowed, invalidated or circumvented, which could limit our ability to stop competitors from marketing similar products or limit the length of term of patent protection we may have for our products, and we may not be able to obtain patent term extension to prolong the terms of the principal patents covering our approved products. Changes in patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection.

In addition, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the value of patents, once obtained, and with regard to our ability to obtain patents in the future. Depending on decisions by the U.S. Congress, the federal courts, and the U.S. Patent and Trademark Office ("PTO"), the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Our patents also may not afford us protection against competitors with similar technology. Because patent applications in the United States and many foreign jurisdictions are typically not published until eighteen months after filing, or in some cases not at all, and because publications of discoveries in the scientific literature often lag behind actual discoveries, neither we nor our licensors can be certain that others have not filed or maintained patent applications for technology used by us or covered by our pending patent applications without our being aware of these applications.

We exclusively license patents and patent applications for inclisiran. The patents covering inclisiran are currently set to expire at various dates.

Inclisiran. We have exclusively licensed from Alnylam patents and patent applications covering RNAi therapeutics targeting PCSK9 for the treatment of hypercholesterolemia and other human diseases for purposes of developing and commercializing such RNAi therapeutics. In November 2018, the PTO issued U.S. Patent No. 10,125,369 ("369 patent"). The '369 patent contains claims directed to specific compositions of the inclisiran product we are developing and methods of administrating such compositions and is set to expire in August 2034 (not including any patent term or pediatric extensions). In addition, some of the patents licensed from Alnylam are directed to general RNAi technology, RNAi compositions including compositions of the inclisiran product, and methods of treatment using such RNAi compositions, which expire between 2020 and 2029 in the United States. In addition, we and Alnylam have filed and are prosecuting a number of patent applications in the United States and in certain foreign countries.

We plan to file applications for patent term extension for inclisiran upon its approval. If we do not receive patent term extensions for the periods requested by us or at all, our patent protection for inclisiran could be limited.

With respect to the portfolio of patents licensed from Alnylam, it is possible that one or more companies hold patent rights that could be asserted against us or patent rights to which we may need a license. If a court rules that we infringe such patent rights that have been asserted against us and/or we are not able to obtain a license on reasonable terms, we may be forced to pay license fees set by the court or may be unable to market inclisiran, which in either case could have a material adverse effect on our business. For example, in October 2017 Silence Therapeutics plc and Silence Therapeutics GmbH, which we refer to together as Silence, served a claim in the High Court of Justice, Chancery Division, Patents Court in the United Kingdom, naming The Medicines Company UK Ltd., our wholly owned subsidiary, Alnylam and Alnylam UK Limited, as co-defendants. In Silence's claim, it sought a determination that it is entitled to supplementary protection certificates ("SPCs"), based on its

European Patent No. 2,258,847 ("847 patent"), and the prospective European regulatory approvals for inclisiran and for certain of Alnylam's product candidates. This was based on Silence's assertion that inclisiran and the cited Alnylam product candidates fall within the scope of the '847 patent. Following briefing and additional claims by the parties, the High Court had listed the trial for 10 days which was to be heard in a window starting on December 3, 2018 for all claims between Silence, Alnylam and us. However, on June 29, 2018, Silence withdrew the proceedings it issued against us seeking a determination that it is entitled to SPCs based on the '847 patent and the prospective European regulatory approvals for inclisiran. The trial between Silence and Alnylam was scheduled to continue without us and to be heard in December 2018. On December 9, 2018, Silence and Alnylam entered into a settlement and license agreement pursuant to which Alnylam received a global license to Silence's relevant intellectual property for all current and future Alnylam products, including inclisiran, for a low royalty on Alnylam's ONPATTRO product in the European Union through 2023. The settlement does not contain any milestones or royalties payments due to Silence with respect to inclisiran. In connection with the settlement, we entered into an agreement with Alnylam and Silence to discontinue all of our pending litigation against Silence and the European Patent Office ("EPO") oppositions of Silence's patents, and we agreed to forgo any reimbursement of legal costs from Silence. Under our collaboration agreement with Alnylam, we received a license from Alnylam covering the license rights granted to Alnylam from Silence with no additional milestone payments or royalties. See "Legal Proceedings" under the Business section of this prospectus supplement for a full description of our litigation with Silence.

In addition to seeking to enforce our patent rights, we have in the past and may in the future seek to enforce our other intellectual property rights, including, for example, our trademark rights in order to prevent third parties from using the same or confusingly similar trademarks. We may not be successful in enforcing such rights and preventing such use. Further, certain of our trademark rights are licensed to us by third parties and, in certain circumstances, on a non-exclusive basis, which does not afford us the right to prevent third parties from using such trademarks. Failure to adequately pursue and enforce our intellectual property rights could damage our brands, enable others to compete with our products and impair our competitive position.

If we are not able to keep our trade secrets confidential, our technology and information may be used by others to compete against us.

We rely significantly upon unpatented proprietary technology, information, processes and know-how. We seek to protect this information by confidentiality agreements and invention assignment agreements with our employees, consultants and other third-party contractors, as well as through other security measures. We may not have adequate remedies for any breach by a party to these confidentiality agreements or invention assignment agreements. In addition, our competitors may learn or independently develop our trade secrets. If our confidential information or trade secrets become publicly known, they may lose their value to us.

If we infringe or are alleged to infringe intellectual property rights of third parties, our business may be adversely affected.

Our research, development and commercialization activities, as well as any product candidates or products resulting from these activities, may infringe or be claimed to infringe patents or patent applications under which we do not hold licenses or other rights. Third parties may own or control these patents and patent applications in the United States and abroad. These third parties could bring claims against us or our collaborators that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages. Further, if a patent infringement suit were brought against us or our collaborators, we or they could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit.

As a result of patent infringement claims, or in order to avoid potential claims, we or our collaborators may choose or be required to seek a license from the third party and be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our collaborators were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we or our collaborators are unable to enter into licenses on acceptable terms. This could harm our business significantly.

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. In addition to infringement claims against us, we may become a party to other patent litigation and other proceedings, including reexamination, inter partes review, post-grant review, and interference proceedings declared by the PTO and opposition proceedings in the EPO, regarding intellectual property rights with respect to our products and technology. Patent litigation and other proceedings may also absorb significant management time. The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Cyber security breaches and other disruptions could compromise our information and expose us to liability, which would cause our business and reputation to suffer.

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect and store confidential and sensitive electronic information on our networks and in our data centers. This information includes, among other things, our intellectual property and proprietary information, the confidential information of our collaborators and licensees, and the personally identifiable information of our employees. It is important to our operations and business strategy that this electronic information remains secure and is perceived to be secure. The size and complexity of our information technology systems, and those of third-party vendors with whom we contract, and the volume of data we retain, make such systems potentially vulnerable to breakdown, malicious intrusion, security breaches and other cyber-attacks. Information security risks have significantly increased in recent years in part due to the proliferation of new technologies and the increased sophistication and activities of organized crime, hackers, terrorists and other external parties, including foreign state actors. Network and information systems-related events affecting our systems, or those of third parties upon which our business relies, such as computer compromises, cyber threats and attacks, computer viruses, worms or other destructive or disruptive software, process breakdowns, denial of service attacks, malicious social engineering or other malicious activities, or any combination of the foregoing, as well as power outages, equipment failure, natural disasters (including extreme weather), terrorist activities, war, human or technological error or malfeasance that may affect such systems, could result in disruption of our business and/or loss, corruption or improper disclosure of personal data, business information, including intellectual property, or other confidential information. In addition, any design or manufacturing defects in, or the improper implementation of, hardware or software applications we develop or procure from third parties could unexpectedly compromise information security.

A security breach or privacy violation that leads to disclosure or modification of or prevents access to personally identifiable information or other protected information could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect personal data, resulting in

increased costs or loss of revenue. Similarly, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If we are unable to prevent such security breaches or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer loss of reputation, financial loss and other regulatory penalties because of lost or misappropriated information.

We have not experienced any material losses to date relating to cyber-attacks or other information security breaches, but there can be no assurance that we will not incur such losses in the future. While we have developed and implemented security measures and internal controls that are designed to protect personal data, business information, including intellectual property, and other confidential information, to prevent data loss, and to prevent or detect security breaches, such security measures cannot provide absolute security and may not be successful in preventing these events from occurring, particularly given that techniques used to access, disable or degrade service, or sabotage systems change frequently, and any network and information systems-related events could require us to expend significant resources to remedy such event.

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

We may receive, generate and store sensitive information, such as employee and patient data. In addition, we actively seek access to medical information, including patient data, through research and development partnerships and collaborations or otherwise. We have legal and contractual obligations regarding the protection of confidentiality and appropriate use of personal data. We and any potential collaborators may be subject to federal, state, local and foreign laws and regulations that apply to the collection, use, retention, protection, disclosure, transfer and other processing of personal data. 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, 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 federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"). Depending on the facts and circumstances, we could be subject to civil, criminal and administrative penalties if we 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.

Several foreign jurisdictions, including the European Union, its member states, among others, have adopted legislation and regulations that increase or change the requirements governing the collection, use, disclosure and transfer of the personal information of individuals in these jurisdictions. In the United States, the state of California enacted legislation, the California Consumer Privacy Act ("CCPA"), effective January 1, 2020, that increases the requirements governing the collection, use, disclosure and transfer of the personal information of individuals in the state of California. These laws and regulations are complex and change frequently, at times due to changes in political climate, and existing laws and regulations are subject to different and conflicting interpretations, which adds to the complexity of processing personal data from these jurisdictions. These laws have the potential to increase costs of compliance, risks of noncompliance and penalties for noncompliance. The Regulation 2016/679, known as the General Data Protection Regulation ("GDPR"), as well as European Union member state implementing legislations, apply to the collection and processing of

personal data, including health-related information, by companies located in the European Union, or in certain circumstances, by companies located outside of the European Union and processing personal information of individuals located in the European Union. These laws impose strict obligations on the ability to process personal data, including health-related information, in particular in relation to their collection, use, disclosure and transfer. For example, the GDPR prohibits the transfer of personal data to countries outside of the European Economic Area, such as the United States, which are not considered by the European Commission to provide an adequate level of data protection. Although there are legal mechanisms to allow for the transfer of personal data from the EEA to the United States, they are subject to legal challenges and uncertainty about compliance with European Union data protection laws remains. The GDPR has increased our responsibility and liability in relation to personal data that we process, and we may be required to put in place additional potential mechanisms to ensure compliance with the new European Union data protection rules.

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.

Risks Related to Our Common Stock and this Offering

Fluctuations in our operating results could affect the price of our common stock.

Our operating results may vary from period to period based on factors, including the timing, expenses and results of clinical trials, announcements regarding clinical trial results and product introductions by us or our competitors, the availability and timing of third-party reimbursement, sales and marketing expenses and the timing of regulatory approvals. If our operating results do not meet the expectations of investors and securities analysts as a result of these or other factors, the trading price of our common stock will likely decrease.

The capped call transactions we entered into in connection with the 2023 Notes may affect the price of our common stock.

In connection with the sale of the 2023 Notes, we entered into capped call transactions with the initial purchasers of the 2023 Notes, their affiliates and other financial institutions, whom we refer to as hedge counterparties.

In connection with establishing their hedges of the capped call transactions, the hedge counterparties or their affiliates entered into various derivative transactions with respect to our common stock. These parties may modify their hedge positions in the future by entering into or unwinding various derivatives with respect to our common stock and/or purchasing or selling our common stock or other securities of ours in the secondary market transactions prior to the maturity of the 2023 Notes (and are likely to do so during any observation period related to a conversion father 2023 Notes). These activities could cause a decrease or avoid an increase in the market price of our common stock.

We are subject to counterparty risk with respect to the capped call transactions.

The counterparties to the capped call transactions we entered into in connection with the issuance of our 2023 Notes are financial institutions (including affiliates of J.P. Morgan Securities LLC), and we will be subject to the risk that the counterparties might default under the capped call transactions. Our exposure to the credit risk of the counterparties will not be secured by any collateral. Global economic conditions have from time to time resulted in the actual or perceived failure or financial difficulties of many financial institutions, including the bankruptcy filing by Lehman Brothers Holdings Inc. and its various affiliates. If a counterparty becomes subject to insolvency proceedings, we will become an unsecured creditor in those proceedings with a claim equal to our exposure at that time under our transactions with that counterparty. Our exposure will depend on many factors but, generally, the increase in our exposure will be correlated to the increase in the market price and in the volatility of our common stock. In addition, upon a default by a counterparty, we may suffer adverse tax consequences and more dilution than we currently anticipate with respect to our common stock. We can provide no assurances as to the financial stability or viability of any counterparty. These activities could cause a decrease or avoid an increase in the market price of our common stock.

Our stock price has been and may in the future be volatile.

This volatility may make it difficult for you to sell common stock when you want or at attractive prices. Our common stock has been and in the future may be subject to substantial price volatility. From January 1, 2015 to June 21, 2019, the last reported closing price of our common stock ranged from a high of $55.95 per share to a low of $16.69 per share. The value of your investment could decline due to the effect upon the market price of our common stock of any of the following factors, many of which are beyond our control:

- announcements of results of clinical trials or nonclinical studies by us or third parties relating to inclisiran or products of our competitors or of regulatory proceedings by us or our competitors;
- approval or rejection of submissions for marketing approval for inclisiran;
- changes in securities analysts' estimates of our financial performance;
- changes in valuations of similar companies;
- variations in our operating results;
- acquisitions and strategic partnerships;
- announcements of technological innovations or new commercial products by us or our competitors or the filing of ANDAs, NDAs or biologics license application for products competitive with ours;
- changes in governmental regulations;
- developments in patent rights or other proprietary rights;
- the extent to which our products are commercially successful globally;
- developments in our ongoing litigation and significant new litigation;
- developments or issues with our contract manufacturers;
- changes in our management; and
- general market conditions.

We believe that period-to-period comparisons of our financial results will not necessarily be indicative of our future performance. If our revenues in any particular period do not meet expectations,

we may not be able to adjust our expenditures in that period, which could cause our operating results to suffer. If our operating results in any future period fall below the expectations of securities analysts or investors, our stock price may fall by a significant amount. The stock markets in general, and the Nasdaq Global Select Market and the market for biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations recently. These fluctuations often have been unrelated or disproportionate to the operating performance of these companies. These broad market and industry factors may adversely affect the market price of our common stock, regardless of our actual operating performance.

Our corporate governance structure, including provisions in our certificate of incorporation and by-laws and Delaware law, may prevent a change in control or management that security holders may consider desirable.

The General Corporation Law of the State of Delaware and our certificate of incorporation and by-laws contain provisions that might enable our management to resist a takeover of our company or discourage a third party from attempting to take over our company. These provisions include:

- Section 203 of the Delaware General Corporation Law, which provides that we may not enter into a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in the manner prescribed in Section 203;
- our board of directors has the authority to issue, without a vote or action of stockholders, up to 5,000,000 shares of a new series of preferred stock and to fix the price, rights, preferences and privileges of those shares, each of which could be superior to the rights of holders of our common stock;
- our directors may be removed with or without cause by the affirmative vote of the holders of at least 75% of the votes which all stockholders would be entitled to cast in any annual election of directors;
- the size of our board of directors is determined by resolution of the board of directors;
- any vacancy on our board of directors, however occurring, including a vacancy resulting from an enlargement of our board, may only be filled by vote of a majority of our directors then in office, even if less than a quorum;
- only our board of directors may call special meetings of stockholders;
- our by-laws may be amended, altered or repealed by (i) the affirmative vote of a majority of our directors, subject to any limitations set forth in the by-laws, or (ii) the affirmative vote of the holders of at least 75% of the votes which all the stockholders would be entitled to cast in any annual election of directors;
- stockholders must provide us with advance notice, and certain information specified in our by-laws, in connection with nominations or proposals by such stockholder for consideration at an annual meeting;
- stockholders may not take any action by written consent in lieu of a meeting; and
- our certificate of incorporation may only be amended or repealed by the affirmative vote of a majority of our directors and the affirmative vote of the holders of at least 75% of the votes which all the stockholders would be entitled to cast in any annual election of directors (and plus any separate class vote that might in the future be required pursuant to the terms of any series of preferred stock that might be outstanding at the time any of these amendments are submitted to stockholders).

These provisions could have the effect of delaying, deferring, or preventing a change in control of us or a change in our management that stockholders may consider favorable or beneficial. These provisions could also discourage proxy contests and make it more difficult for stockholders to elect directors and take other corporate actions. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock or our other securities.

Our business could be negatively affected as a result of the actions of activist shareholders.

Proxy contests have been waged against many companies in the biopharmaceutical industry over the last few years. If faced with a proxy contest, we may not be able to successfully defend against the contest, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest because:

- responding to proxy contests and other actions by activist shareholders may be costly and time-consuming and may disrupt our operations and divert the attention of management and our employees;
- perceived uncertainties as to our future direction may result in our inability to consummate potential acquisitions, collaborations or in-licensing opportunities and may make it more difficult to attract and retain qualified personnel and business partners; and
- if individuals are elected to our board of directors with a specific agenda different from ours, it may adversely affect our ability to effectively and timely implement our strategic plan and create additional value for our stockholders.

Sales of additional shares of our common stock, including by us of our directors and officers following expiration or early release of the lock-up, could cause the price of our common stock to decline.

Sales of substantial amounts of our common stock in the public market, or the availability of such shares for sale, by us or others, including the issuance of common stock upon exercise of outstanding options, could adversely affect the price of our common stock. In connection with this offering, we have agreed to a lock-up for a period of 90 days following this offering, and our directors and officers have entered into lock-up agreements for a period of 90 days following this offering. We and our directors and officers may be released from lock-up prior to the expiration of the lock-up period at the discretion of Goldman Sachs & Co. LLC and J.P. Morgan Securities LLC on behalf of the underwriters. See "Underwriting." Upon expiration or earlier release of the lock-up, we and our directors and officers may sell shares into the market, which could adversely affect the market price of shares of our common stock. In addition, during the lock-up period and thereafter, sales of shares held by our directors and officers are permitted under trading plans, as in effect as of the date of the applicable lock-up agreement, established pursuant to Rule 10b5-1 of the Exchange Act.

USE OF PROCEEDS

We estimate that the net proceeds we will receive from this offering will be approximately $140.7 million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and based on an assumed public offering price of $36.40, the last sale price of our common stock on June 21, 2019 as reported on the NASDAQ Global Select Market. If the underwriters exercise their option to purchase additional shares in full, we estimate that the net proceeds to us will be approximately $161.9 million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering to fund our development of inclisiran and for general corporate purposes. General corporate purposes may include the acquisition of complementary products, technologies or businesses, repayment and refinancing of debt, pre-commercial activities, working capital and capital expenditures. We may temporarily invest the net proceeds in investment-grade, interest-bearing securities until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We anticipate that we will retain all of our future earnings, if any, for use in the expansion and operation of our business and do not anticipate paying cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our board of directors.

BUSINESS

Our Company

Overview

We are a biopharmaceutical company driven by our purpose to solve major medical, societal and economic challenges in healthcare. We have a singular focus on one of the greatest global healthcare challenges and burdens—that presented by atherosclerotic cardiovascular disease ("ASCVD"), which remains the number one cause of death in the United States and worldwide. We take on that challenge by developing inclisiran, the investigational RNA interference ("RNAi") therapeutic, that specifically inhibits production of proprotein convertase subtilisin/kexin type 9 ("PCSK9"), a key protein that controls LDL-cholesterol ("LDL-C") levels. We believe inclisiran is uniquely suited to make a significant difference reducing risk in ASCVD. We have the right to develop, manufacture and commercialize inclisiran under our collaboration agreement with Alnylam.

On August 22, 2018, we completed the sale of our rights to branded Angiomax in the United States to Sandoz for $9.9 million. Following such divestiture, we no longer market any products. Historically, our revenues have been generated primarily from sales of Angiomax in the United States, but competition from generic versions of Angiomax following the loss of market exclusivity in the United States in July 2015 and in Europe in August 2015 resulted in a significant decline in revenue from Angiomax prior to our divestiture of the product. Based on our current business, we expect to incur net losses for the foreseeable future.

Inclisiran

Overview

Inclisiran is a subcutaneously administered small interfering RNA ("siRNA"), that prevents the production of PCSK9 and is being developed as a potential treatment for hypercholesterolemia. siRNA therapy harnesses a natural mechanism called RNAi. We obtained global rights to this product candidate under a license and collaboration agreement that we entered into with Alnylam in February 2013 to develop, manufacture and commercialize RNAi therapeutics targeting the PCSK9 gene for the treatment of hypercholesterolemia and other human diseases. RNAi is a natural mechanism within cells to selectively prevent the production of specific proteins. PCSK9 is a protein involved in the regulation of low-density lipoprotein ("LDL"), receptor levels on cells in the liver (hepatocytes) responsible for cholesterol clearance. Inclisiran prevents the production of PCSK9 and lowers LDL-C levels.

PCSK9 and PCSK9 inhibition

PCSK9, a member of the serine protease family, plays a key role in controlling the levels of LDL receptors on the surface of certain liver cells called hepatocytes. PCSK9 is expressed and secreted into the bloodstream predominantly by the liver, binds LDL receptors both intracellularly and extracellularly and promotes the lysosomal degradation of these receptors in hepatocytes. By reducing the available LDL receptor pool on the surface of hepatocytes, PCSK9 increases circulating LDL-C levels. People with naturally occurring variants in the PCSK9 gene and consequently lower PCSK9 protein activity have reduced serum LDL-C levels and lower risk for coronary heart disease, with no apparent negative health consequences.

RNA interference

RNAi is a natural process within cells to prevent the production of specific proteins and represents a promising aspect of biology and drug development today. Its discovery was recognized with the award of the 2006 Nobel Prize for Physiology or Medicine. siRNAs are the molecules that mediate RNAi within cells, and siRNA therapies such as inclisiran harness the natural RNAi process. siRNAs function

upstream of today's medicines by targeting the root cause of diseases. This approach has the potential to transform the care of patients.

Clinical Development

Overview

Under our global license and collaboration agreement with Alnylam, we and Alnylam initially collaborated on the development of inclisiran and ALN-PCS02, an intravenously administered earlier siRNA therapy. Alnylam was responsible for the development of these product candidates until Phase 1 was completed. We have assumed the responsibility for the further development and commercialization of all product candidates under our agreement with Alnylam. In October 2013, we and Alnylam selected a lead subcutaneously administered development candidate, now referred to as inclisiran, for development for the potential to lower LDL-C. In December 2014, under the terms of our agreement with Alnylam, Alnylam initiated a Phase 1 clinical trial of inclisiran in the United Kingdom. Data from the Phase 1 trial was presented at the European Society of Cardiology meeting in August 2015 and at the American Heart Association meeting in November 2015, and was published in the New England Journal of Medicine.

In January 2016, we began enrolling patients in the ORION-1 Phase 2 dose finding trial. ORION-1 was a placebo-controlled, double-blind, randomized trial of single or multiple subcutaneous injections of inclisiran in a total of 501 patients with ASCVD or ASCVD-risk equivalents (e.g., diabetes and familial hypercholesterolemia), and elevated LDL-C despite maximally tolerated LDL-C lowering therapies. The study compared the effect of different doses of inclisiran and evaluated the potential for an infrequent dosing regimen. The primary endpoint of the study was the percentage change in LDL-C from baseline at Day 180.

In March 2017, we reported positive final results from the ORION-1 Phase 2 study of inclisiran. Efficacy data presented reaffirmed inclisiran's significant LDL-C lowering effects. Administration of 284 mg of inclisiran (300 mg inclisiran sodium) on Day-1 and Day-90 lowered the mean LDL-C by an average of 52.6% and up to 81% at Day-180. For the subsequent six-month period, from Day-90 to Day-270, the time-averaged LDL-C reduction was 51%. These robust data underscore the potential of a six-monthly maintenance regimen, which is currently being evaluated in the inclisiran Phase 3 clinical program. No material safety issues were observed on inclisiran in ORION-1, which demonstrated an adverse event profile similar to placebo.

We developed a dose-pharmacodynamic ("dose-PD"), response model based on the ORION-1 data to perform modeling and simulation experiments to support the selection of the Phase 3 dose and dose regimen. The dose-PD modeling and simulation supported the clinical observations from ORION-1 that a 300 mg dose given subcutaneously on Day-1, Day-90 and every six months thereafter is the optimal dose and dose regimen for further development in Phase 3. This dose and dose regimen maintains a time-averaged LDL-C reduction of >50%. Our initial Phase 3 program, described below, will test this dose and dose regimen in patients with ASCVD, ASCVD-risk equivalents, or familial hypercholesterolemia ("FH"). Further dose-PD response modeling and simulation demonstrated that a 300 mg dose given once a year would result in a time-averaged LDL-C reduction of approximately 43-45%. We believe that this once a year dose regimen of 300 mg of inclisiran could be tested in patient populations at lower cardiovascular risk for whom daily oral tablets remain a challenge.

In January 2017, we initiated the ORION-2 and ORION-3 studies. ORION-2 is a pilot study to examine the efficacy, safety and tolerability of inclisiran in a limited number of patients with homozygous FH, to support further evaluation in the larger ORION-5 trial (described below). The ORION-3 study is an open label extension study of ORION-1 with the objective to evaluate the efficacy, safety and tolerability of long-term dosing of inclisiran. ORION-3 will also assess the feasibility

of switching to inclisiran from evolocumab (trade named Repatha) on certain clinical and patient-reported endpoints.

In May 2019, we obtained new long-term data from the ORION-3 study, showing that twice-a-year dosing with inclisiran consistently resulted in more than 50% lower LDL cholesterol after 3 years. In addition, no material safety issues were observed with 3 years of follow-up in the study. ORION-3 shows no change in the overall safety profile compared to the one-year follow-up in ORION-1.

Phase 3 Clinical Program—ORION 5, 9, 10 and 11 clinical trials.

In the fourth quarter of 2017, we initiated the Phase 3 LDL-C lowering program for inclisiran. The Phase 3 program is comprised of four pivotal clinical trials in patients with ASCVD, ASCVD-risk equivalents, heterozygous FH, and homozygous FH. We anticipate that data from three trials, ORION-9, ORION-10 and ORION-11, will support the submission of a new drug application ("NDA"), in the United States and a marketing authorization application ("MAA"), in the European Union at or around the end of 2019. In the ORION-9, ORION-10 and ORION-11 trials, patients will be studied for 18 months and inclisiran 284 mg (inclisiran sodium 300 mg) will be given subcutaneously on Day-1, Day-90 and every six months thereafter for a total of four doses during the 18-month study period. As of June 20, 2019, more than 3,300 subjects had received a fourth dose of inclisiran or placebo in the ORION 9, ORION-10 and ORION-11 trials. We expect to start reporting Phase 3 data readouts in the second half of the third quarter of 2019. We expect patients in the ORION-5 trial of inclisiran in patients with homozygous FH to have a shorter comparative treatment window than the patients in the other ORION Phase 3 trials. The four Phase 3 clinical trials are further described below:

Study	Sites	Main inclusion criteria	Patients
ORION-5	US, EU, South Africa (SA)	Homozygous familial hypercholesterolemia ("HoFH")	45 (estimated)
ORION-9	US, EU, SA	Heterozygous familial hypercholesterolemia ("HeFH")	482
ORION-10	US	ASCVD	1,561
ORION-11	EU, SA	ASCVD and risk equivalent patients	1,617
			3,705

ORION-5 is a two-part (double-blind, placebo-controlled/open label) multicenter study to evaluate safety, tolerability, and efficacy of inclisiran in approximately 45 subjects with HoFH. We commenced enrollment in the ORION-5 trial in February 2019. On January 23, 2018, the FDA granted orphan drug designation for inclisiran for the treatment of HoFH. ORION-9 is a placebo-controlled, double-blind, randomized study of inclisiran versus placebo (1:1) in approximately 482 patients with HeFH. The primary endpoint of ORION-9 study is LDL-C reduction from baseline at Day-510. The ORION-9 trial commenced in November 2017. In February 2018, we announced that this trial had exceeded its target enrollment of 400 patients.

ORION-10 is a placebo-controlled, double-blind, randomized study of inclisiran versus placebo (1:1) in approximately 1,561 patients with ASCVD and LDL-C levels above 70 mg/dL despite maximum tolerated doses of LDL-C lowering therapies including statins. The primary endpoint of ORION-10 study is LDL-C reduction from baseline at Day-510. The ORION-10 trial commenced in November 2017 and in March 2018, we announced that this trial had exceeded its target enrollment of 1,500 patients.

ORION-11 is a placebo-controlled, double-blind, randomized study of inclisiran versus placebo (1:1) in approximately 1,617 patients with ASCVD or ASCVD-risk equivalents and elevated LDL-C levels above 70 mg/dL or 100 mg/dL, respectively, despite maximum tolerated doses of LDL-C lowering

therapies including statins. The primary endpoint of the study is LDL-C reduction from baseline at Day-510. The ORION-11 trial commenced in November 2017. In January 2018, we announced that this trial had exceeded its target enrollment of 1,500 patients.

Cardiovascular Outcomes Trial—ORION-4

We are also conducting a cardiovascular outcomes trial in approximately 15,000 patients with ASCVD on a background of standard-of-care lipid-lowering therapy (usually high intensity statins), to determine the effects of inclisiran on cardiovascular outcomes. We initiated enrollment in the trial in October 2018. The overall design of the ORION-4 outcomes trial has been agreed to with the FDA and EMA. The ORION-4 study will be conducted in close collaboration with the academic groups, Clinical Trial Service Unit and Epidemiological Studies Unit of the University of Oxford and Thrombolysis In Myocardial Infarction (TIMI) Study Group of the Brigham and Women's Hospital, Boston, Massachusetts, as well as other scientific experts. The primary efficacy endpoint of the trial will be a composite endpoint of coronary heart disease death, non-fatal myocardial infarction, fatal or non-fatal ischemic stroke and urgent coronary revascularization. These endpoints have been demonstrated to be modifiable in previous, similar outcomes trials with lipid modifying therapies. The duration of the outcomes trial will be long enough, with a median of four to five years follow-up, to accumulate a sufficient number of events to ascertain treatment group differences and demonstrate the maximum clinical effect size associated with LDL-C lowering. We anticipate that, if inclisiran is approved for sale and the outcomes trial is successful, we will submit the results of the outcomes trial to the FDA as a supplemental New Drug Application ("sNDA"), and as a variation to the MAA with the European Medicines Agency ("EMA").

Medical Need

Despite advances in treatment, cardiovascular disease is the leading cause of death worldwide, resulting in over 18 million deaths annually. Eighty-five percent of all cardiovascular disease deaths are due to coronary heart disease or strokes. Not merely a disease of the elderly, cardiovascular disease is responsible for more than a third of the 17 million premature deaths annually worldwide, causing substantial losses in economic productivity.

Elevated LDL-C is the primary cause of ASCVD and the most readily modifiable risk factor, and of itself a major cause of years of life lost. Overwhelming evidence demonstrates that reducing LDL-C directly leads to improved cardiovascular outcomes, the clinical risk reduction is linearly-proportional to absolute LDL-C reduction, with each 39 mg/dL reduction in LDL-C yielding a 22% reduction in major coronary events after 12 months of continuous treatment.

Approximately 100 million people worldwide are treated with lipid lowering therapies, predominantly statins, to reduce LDL-C and the associated risk of death, nonfatal myocardial infarction and nonfatal stroke or associated events. Yet cardiovascular disease remains the leading cause of death, highlighting the unmet medical need for additional treatment options for lowering LDL-C. Statins are effective, but are associated with well-known limitations. First, high-intensity oral therapies do not get all patients to LDL-C goals. This is particularly important in patients with pre-existing coronary heart disease, familial hypercholesterolemia, and/or diabetes, who are at the highest risk and require the most intensive management. Second, not all patients tolerate statins and many are unable to tolerate them at sufficiently high doses. Third, observational studies have demonstrated that >50% of patients do not adhere to oral therapies including statins for more than six months, leaving them completely unprotected against risk of cardiovascular events, including death.

We believe that new long-acting treatment with significant, durable lowering of LDL-C can fulfill important unmet efficacy needs in ASCVD treatment and prevention. Clinical studies performed with inclisiran have demonstrated reductions in LDL-C by more than 50%, when given on top of other lipid lowering therapies, and therefore has the potential to meet this unmet need for additional significant

LDL-C reduction. In addition, we believe that inclisiran's twice-a-year dosing administered by a health-care professional aligns with common approaches to care including how often physicians follow up with ASCVD patients. Twice-a-year administration of an LDL-C lowering therapy by a health-care professional can circumvent the challenges of treatment adherence, which has been a significant problem with more frequently dosed therapies and has hampered the ability to make progress against heart disease.

Business Development Strategy

On November 3, 2015, we announced that we were in the process of evaluating our operations with a goal of unlocking and maximizing stockholder value. In particular, we stated our intention was to explore strategies for optimizing our capital structure and liquidity position and to narrow our operational focus by strategically separating non-core businesses and products in order to generate non-dilutive cash and reduce associated cash burn and capital requirements.

As a result of our decision to narrow our operational focus, we have completed the following transactions and are now focused on the development of inclisiran as a transformative treatment for ASCVD:

Sale of Angiomax. On August 22, 2018, we completed the sale of our rights to branded Angiomax in the United States to Sandoz for $9.9 million. Prior to the divestiture, Sandoz had been selling an authorized generic of Angiomax (bivalirudin) as of July 2, 2015 pursuant to a supply and distribution agreement with us. As a result of the divestiture, Sandoz is the holder of the NDA for Angiomax in the United States and will be responsible for manufacturing and supply of Angiomax in the second quarter of 2019. In February 2019, we sold our rights to branded Angiomax in Canada to Sandoz AG for $500,000 and, as a result of the transaction, Sandoz AG is the holder of the marketing authorization for Angiomax in Canada and is responsible for manufacturing and supply of Angiomax.

Sale of Infectious Disease Products. On January 5, 2018, we completed the sale of our infectious disease portfolio, consisting of the products Vabomere, Orbactiv and Minocin IV and line extensions thereof, and substantially all of the assets related thereto, other than certain pre-clinical assets, to Melinta Therapeutics, Inc. ("Melinta"). At the completion of the sale, we received approximately $166.4 million and 3,313,702 shares of Melinta common stock having a market value, based on Melinta's closing share price on March 31, 2019, of approximately $2.4 million. In addition, we are entitled to receive (i) a cash payment that was due 12 months following the closing of the transaction equal to $25 million; (ii) a cash payment payable 18 months following the closing of the transaction equal to $25 million; and (iii) tiered royalty payments of 5% to 25% on worldwide net sales of (a) Vabomere and (b) Orbactiv and Minocin IV, collectively, and Melinta assumed potential milestone payments due under our agreement with Rempex Pharmaceuticals, Inc. ("Rempex"). None of the future payments due from Melinta are secured by collateral and we are currently in litigation with Melinta with respect to its obligations to us. See "Legal Proceedings" below for a description of our litigation related to Melinta.

In October 2018, we divested certain pre-clinical infectious disease assets not acquired by Melinta, which included the funding agreement with the Biomedical Advanced Research and Development Authority ("BARDA"), of the U.S. Department of Health and Human Services ("HHS"). The assets were purchased by Qpex Biopharma, Inc. ("Qpex"), a new company formed by a syndicate of venture firms led by New Enterprise Associates and accompanied by Adams Street Partners, LYZZ Capital, Hatteras Venture Partners and Stanford University Draper Fund. At the completion of the sale, we received approximately $2.8 million and are entitled to receive up to $29 million upon the achievement of certain milestones related to the pre-clinical assets. In addition, Qpex assumed potential milestone payments due under our agreement with Rempex, related to the development of the pre-clinical assets.

Sale of Non-Core Cardiovascular Products. On June 21, 2016, we completed the sale of Cleviprex, Kengreal and rights to Argatroban for Injection, which we refer to collectively as Non-Core ACC Assets, to Chiesi USA, Inc. ("Chiesi USA"), and its parent company Chiesi Farmaceutici S.p.A. ("Chiesi"). Under the terms of the purchase and sale agreement, Chiesi and Chiesi USA acquired our Non-Core ACC Assets and related assets, and assumed substantially all of the liabilities arising out of the operation of the businesses and the acquired assets after closing, including any obligations with respect to future milestones relating to each of the products. At the completion of the sale, we received approximately $263.8 million in cash, which included the value of product inventory, and may receive up to an additional $480.0 million in the aggregate following the achievement of certain specified calendar year net sales milestones with respect to net sales of each of Cleviprex and Kengreal. As part of the transaction to sell Non-Core ACC Assets, we sublicensed to Chiesi all of our rights to Cleviprex and Kengreal under our license from AstraZeneca AB ("AstraZeneca"). Subsequent to the completion of the sale, these sublicenses from us to Chiesi were terminated, Chiesi purchased from AstraZeneca all or substantially all of AstraZeneca's assets relating to Cleviprex and Kengreal, the parties released certain claims against one another, and we paid Chiesi $7.5 million.

Sale of Hemostasis Business. On February 1, 2016, we completed the sale of our hemostasis business, consisting of PreveLeak, Raplixa and Recothrom products to wholly-owned subsidiaries of Mallinckrodt plc ("Mallinckrodt"). Under the terms of the purchase and sale agreement, Mallinckrodt acquired all of the outstanding equity of Tenaxis Medical, Inc. and ProFibrix B.V. and assets exclusively related to the Recothrom product. Mallinckrodt assumed all liabilities arising out of Mallinckrodt's operation of the businesses and the acquired assets after closing, including all obligations with respect to milestones relating to the PreveLeak and Raplixa products. At the completion of the sale, we received approximately $174.1 million in cash from Mallinckrodt, and may receive up to an additional $235.0 million in the aggregate following the achievement of certain specified calendar year net sales milestones with respect to net sales of PreveLeak and Raplixa. The amount paid at closing was subject to a post-closing purchase price adjustment process with respect to the Recothrom inventory and the net working capital of the hemostasis business as of the date of the closing. In the first quarter of 2018, Mallinckrodt announced it would no longer commercialize Raplixa and sold Recothrom and PreveLeak to Baxter International Inc. ("Baxter"), with Baxter assuming the sales milestones associated with PreveLeak.

Alnylam License Agreement. In February 2013, we entered into a license and collaboration agreement with Alnylam to develop, manufacture and commercialize therapeutic products targeting the PCSK9 gene based on certain of Alnylam's RNAi technology. Under the terms of the agreement, we obtained the exclusive, worldwide right under Alnylam's technology to develop, manufacture and commercialize PCSK9 products for the treatment, palliation and/or prevention of all human diseases. We paid Alnylam $25.0 million in an initial license payment and agreed to pay up to $180.0 million in success-based development, regulatory and commercialization milestones. In December 2014, we paid a development milestone payment of $10.0 million based upon the initiation of a Phase 1 clinical trial for inclisiran and in January 2018 we paid a development milestone payment of $20.0 million based upon the initiation of our phase 3 study for inclisiran. In addition, Alnylam will be eligible to receive scaled double-digit royalties based on annual worldwide net sales of PCSK9 products by us or our affiliates and sublicensees. Royalties to Alnylam are payable on a product-by-product and country-by-country basis until the last to occur of the expiration of patent rights in the applicable country that cover the applicable product, the expiration of non-patent regulatory exclusivities for such product in such country, and the twelfth anniversary of the first commercial sale of the product in such country. The royalties are subject to reduction in specified circumstances. We are also responsible for paying royalties, and in some cases milestone payments, owed by Alnylam to its licensors with respect to intellectual property covering these products. Alnylam was responsible for developing the lead product through the end of the first Phase 1 clinical trial and to supply the lead product for the first Phase 1 clinical trial and the first phase 2 clinical trial. Alnylam bore the costs for these activities. We are

responsible for all other development, manufacturing and commercialization activities under the agreement.

Sales and Distribution

Following the divestiture of our rights to branded Angiomax to Sandoz in August 2018, we no longer market any products. Since July 2015, Sandoz had the exclusive right to sell bivalirudin (250 mg/ml) in the United States under our approved NDA for Angiomax but labeled and sold under the Sandoz name, which we refer to herein as authorized generic Angiomax (bivalirudin), pursuant to a supply and distribution agreement we entered into with Sandoz. Prior to the divestiture to Sandoz, we distributed branded Angiomax in the United States through a sole source distribution model with Integrated Commercialization Solutions ("ICS"). ICS then primarily sold branded Angiomax to a limited number of national medical and pharmaceutical wholesalers with distribution centers located throughout the United States. Our agreement with ICS provided that ICS would be our exclusive distributor of branded Angiomax in the United States. Under the terms of this fee-for-service agreement, ICS placed orders with us for sufficient quantities to maintain an appropriate level of inventory based on our customers' historical purchase volumes. ICS assumed all credit and inventory risks, was subject to our standard return policy and had sole responsibility for determining the prices at which it sold these products, subject to specified limitations in the agreement. The agreement was terminated in February 2019.

Historically, we also marketed and sold Angiomax outside the United States, principally through distributor relationships. These distributors included Sandoz Canada Inc., which distributed Angiomax in Canada and currently holds marketing rights to Angiomax in Canada, and affiliates of Grupo Ferrer Internacional who distributed Angiox in Cyprus, Greece, Portugal and Spain and in a number of countries in Central America and South America. We also had agreements with other third parties for other countries outside of the United States. We have discontinued and withdrawn, or are in the process of voluntarily discontinuing and withdrawing, Angiomax from the market outside of North America and have ceased related commercialization activities. We have also entered into a strategic collaboration with SciClone Pharmaceuticals ("SciClone"), under which we granted SciClone a license and the exclusive rights to promote, market and sell Angiomax in China.

Manufacturing

We do not have a manufacturing infrastructure and we do not intend to develop one. We are currently a party to clinical agreements, and are negotiating commercial agreements, with contract manufacturers for the supply of bulk drug substance for inclisiran and with other third parties for the formulation, packaging and distribution of inclisiran. Our product manufacturing operation is comprised of professionals with expertise in pharmaceutical manufacturing, product development, logistics and supply chain management and quality management and supply chain compliance. These professionals oversee the manufacturing and distribution of inclisiran by third-party companies.

Inclisiran

Under our agreement with Alnylam, Alnylam supplied the quantity of finished product required for the conduct of the first Phase 1 clinical trial and the first Phase 2 clinical trial of inclisiran. Alnylam bore the costs of these activities, subject to certain agreed-upon caps. We have the sole right and responsibility to manufacture and supply licensed product for further development and commercialization under our development plan. We and Alnylam entered into a development supply agreement under which Alnylam agreed to transfer the manufacturing technology for the product to us or our third-party manufacturers. We have entered into agreements with two contract manufacturing organizations for the manufacture of clinical supplies of drug substance, and another manufacturing organization for the supply of drug product for use in clinical and non-clinical studies. Subsequent to the completion of Phase 2 all clinical and non-clinical materials have been directly sourced from suppliers by us.

Bulk Drug Substance. On October 27, 2016, we entered into a services and supply agreement with Agilent Technologies ("Agilent"), to supply inclisiran sodium manufactured by a chemical solid phase oligonucleotide based process. Agilent has supplied a number of batches using this process that have been used in drug product manufacture for clinical studies. Further on December 9, 2015, we entered into a services and supply agreement, as amended on July 27, 2016, with Nitto Denko Avecia for the technical transfer and manufacture of inclisiran sodium. We have an agreement with Alnylam for the supply of GalNAc-resin, a key starting material through process validation. Additionally, we and Alnylam are transferring technology and relationships for the manufacturer of GalNAc-resin and associated components to third parties jointly selected by us and Alnylam for the manufacture of commercial supplies of GalNAc-succinate and GalNAc-resin.

Drug Product. On June 3, 2016, we entered into a master service agreement with Alcami Corporation to develop processes and methods for the manufacture of inclisiran drug product. Under the agreement, Alcami has manufactured all of the inclisiran sodium vials and placebo vials used to date in clinical and non-clinical studies.

Additionally, on September 25, 2017, we entered into a technology transfer and manufacturing service agreement with Corden Pharma for the development and manufacture of pre-filled syringes of inclisiran sodium and placebo for use in clinical studies. To date Corden Pharma has manufactured all of the pre-filled syringes used in Phase 3 clinical studies.

Competition

The development and commercialization of new drugs is highly competitive. We face competition from pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Many of our competitors are substantially larger than we are and have substantially greater capital resources, research and development capabilities and experience, and financial, technical, manufacturing, marketing and human resources than we have. Additional mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in our competitors.

In addition, our competitors may develop, market or license products or other novel technologies that are more effective, safer or less costly than any that have been or are being developed by us, or may obtain marketing approval for their products from the FDA or equivalent foreign regulatory bodies more rapidly than we may obtain approval for ours. We expect to compete on the basis of product efficacy, safety, ease of administration, price and economic value compared to drugs used in current practice or currently being developed.

Inclisiran

The market targeting hypercholesterolemia is highly competitive. Inclisiran is being evaluated when given in combination with maximally tolerated first line therapy consisting of HMG-CoA reductase inhibitors, commonly known as statins. If approved, we expect inclisiran to compete with the two currently approved and marketed anti-PCSK9 antibodies, Amgen's Repatha and Sanofi's Praluent, which are indicated for the treatment of hypercholesterolemia in the United States and Europe. In addition, other LDL-C lowering therapies, including PCSK9-targeted approaches, are in development at a number of companies. Oral products that lower LDL-C, if approved, include Bempedoic Acid (ETC-1002), which is being developed by Esperion Therapeutics Inc., and gemcabene, which is being developed by Gemphire Therapeutics Inc. Other RNA-targeted therapies, including antisense oligonucleotides and siRNA therapies, are also in development and may also be competitive with inclisiran, if approved.

Intellectual Property

Our success will depend in part on our ability to protect the products we acquire or license by obtaining and maintaining patent protection both in the United States and in other countries. We rely upon trade secrets, know-how, continuing technological innovations, contractual restrictions and licensing opportunities to develop and maintain our competitive position. We plan to prosecute and defend patents or patent applications we file, acquire or license.

Inclisiran. We have exclusively licensed from Alnylam patents and patent applications covering RNAi therapeutics targeting PCSK9 for the treatment of hypercholesterolemia and other human diseases for purposes of developing and commercializing such RNAi therapeutics. In November 2018, the U.S. Patent and Trademark Office issued U.S. Patent No. 10,125,369, or the '369 patent. The '369 patent contains claims directed to specific compositions of the inclisiran product we are developing and methods of administrating such compositions and is set to expire in August 2034 (not including any patent term or pediatric extensions). In addition, some of the patents licensed from Alnylam are directed to general RNAi technology, RNAi compositions including compositions of the inclisiran product, and methods of treatment using such RNAi compositions, which expire between 2020 and 2029 in the United States. In addition, we and Alnylam have filed and are prosecuting a number of patent applications in the United States and in certain foreign countries.

The patent positions of pharmaceutical and biotechnology firms like us can be uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued. Consequently, we do not know whether any of the patent applications we acquire, license or file will result in the issuance of patents or, if any patents are issued, whether they will provide significant proprietary protection or will be challenged, circumvented or invalidated. Because unissued U.S. patent applications filed prior to November 29, 2000 and patent applications filed within the last 18 months are maintained in secrecy until patents issue, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings declared by the PTO to determine priority of invention, or in opposition proceedings in a foreign patent office. Participation in these proceedings could result in substantial cost to us, even if the eventual outcome is favorable to us. Even issued patents may not be held valid by a court of competent jurisdiction. An adverse outcome could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using such technology.

The development of hypercholesterolemia products and RNAi therapeutics are intensely competitive. A number of pharmaceutical companies, biotechnology companies, universities and research institutions have filed patent applications or received patents in these fields. Some of these patent applications could be competitive with applications we have acquired or licensed, or could conflict in certain respects with claims made under our applications. Such conflict could result in a significant reduction of the coverage of the patents we have acquired or licensed, which would have a material adverse effect on our business, financial condition and results of operations. In addition, if patents are issued to other companies that contain competitive or conflicting claims with claims of our patents and such claims are ultimately determined to be valid, we may not be able to obtain licenses to these patents at a reasonable cost, or develop or obtain alternative technology.

We also rely on trade secret protection for our confidential and proprietary information. However, others may independently develop substantially equivalent proprietary information and techniques. Others may also otherwise gain access to our trade secrets or disclose such technology. We may not be able to meaningfully protect our trade secrets.

It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of

employment or consulting relationships with us. These agreements generally provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees and consultants, the agreements provide that all inventions conceived by the individual shall be our exclusive property. These agreements may not provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

We have a number of trademarks that we consider important to our business. The Medicines Company® name and logo are either our registered trademarks or our trademarks in the United States and other countries. We have also registered some of these marks in a number of foreign countries. Although we have a foreign trademark registration program for selected marks, we may not be able to register or use such marks in each foreign country in which we seek registration. We believe that our products are identified by our trademarks and, thus, our trademarks are of significant value. Each registered trademark has a duration of 10 to 15 years, depending on the date it was registered and the country in which it is registered, and is subject to an infinite number of renewals for a like period upon continued use and appropriate application. We intend to continue the use of our trademarks and to renew our registered trademarks based upon each trademark's continued value to us.

Customers

In the United States, we sold branded Angiomax, until our divesture of the products to Sandoz in August 2018, to our sole source distributor, ICS. At December 31, 2017, amounts due from ICS represented approximately $2.9 million, or 27%, of gross accounts receivable. We also had a supply and distribution arrangement with Sandoz under which Sandoz sold authorized generic Angiomax (bivalirudin) in the United States. We generated total net revenue under the sales and distribution arrangement with Sandoz by making products sales to Sandoz and received royalty payments from Sandoz in respect of Sandoz's sales of authorized generic Angiomax (bivalirudin). Product sales and royalty revenues from Sandoz accounted for 143% and 81% of our net revenues for 2018 and 2017, respectively. At December 31, 2017, amounts due from Sandoz represented approximately $5.1 million or 48.2%, of gross accounts receivable.

Government Regulation

Government authorities in the United States and other countries extensively regulate the research, testing, manufacturing, labeling, safety, advertising, promotion, storage, sales, distribution, import, export and marketing, among other things, of our products and product candidates. In the United States, the FDA regulates drugs and biologics, under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act respectively and their implementing regulations. We cannot market or commercially distribute a drug until we have submitted an application for marketing authorization to the FDA, and the FDA has approved it. Both before and after approval is obtained, violations of regulatory requirements may result in various adverse consequences, including, among other things, clinical holds, untitled letters, warning letters, fines and other monetary penalties, the FDA's delay in approving or refusal to approve a product, product recall or seizure, suspension or withdrawal of an approved product from the market, interruption of production, operating restrictions, injunctions and the imposition of civil or criminal penalties. The steps required before a drug may be approved by the FDA and marketed in the United States generally include:

- pre-clinical laboratory tests, animal studies and formulation studies;
- submission to the FDA of an investigational new drug application ("IND") for human clinical testing, which must become effective before human clinical trials may begin;

- adequate and well-controlled clinical trials to establish the safety and efficacy of the drug for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practices ("cGMP"); and
- FDA review and approval of the NDA.

Pre-Clinical Tests

Pre-clinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. The results of the pre-clinical tests, together with manufacturing information, analytical data, clinical study protocol(s), and other information, are submitted to the FDA as part of an IND, which must become effective before human clinical trials in the United States may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA puts the trial on clinical hold because of concerns or questions about issues such as the design of the clinical trial(s) or the safety of the drug for administration to humans. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. Submission of an IND does not necessarily result in the FDA allowing clinical trials to commence. In addition, the FDA may impose a clinical hold at any time which includes during an ongoing clinical trial if, for example, safety concerns arise, in which case the trial cannot recommence without the FDA's authorization. A clinical hold can result in a substantial delay and expense.

Clinical Trials

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring subject safety, and the effectiveness criteria, or endpoints, to be evaluated. Each protocol intended to study investigational new drugs in the United States must be submitted to the FDA as part of the IND, and the FDA may or may not allow that trial to proceed. Each trial also must be reviewed and approved by an independent Institutional Review Board ("IRB"), at each proposed study site before it can begin.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined.

- Phase 1 usually involves the initial introduction of the investigational drug into people to evaluate its safety, dosage tolerance, pharmacokinetics, and, if possible, to gain an early indication of its effectiveness.
- Phase 2 usually involves trials in a limited patient population to: evaluate dosage tolerance and appropriate dosage; identify possible adverse effects and safety risks; and evaluate preliminarily the efficacy of the drug for specific indications.
- Phase 3 trials usually involve administration of the drug to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to evaluate safety, and statistically evaluate the efficacy of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

We cannot guarantee that Phase 3 testing of inclisiran will be completed successfully within any specified period of time, if at all. Furthermore, we, the IRB, or the FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

Sponsors are required to publicly disseminate information about ongoing and completed clinical trials on a government website administered by the National Institutes of Health ("NIH"), and are subject to civil money penalties and other civil and criminal sanctions for failing to meet these obligations.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the pre-clinical studies and of the clinical studies, together with other detailed information, including information on the manufacture and composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. The submission of an NDA typically requires the payment of a significant user fee to FDA. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission before accepting them for filing to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. If the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Before approving an application, the FDA usually will inspect the facility or the facilities at which the drug is manufactured, and will not approve the product unless cGMP compliance is satisfactory. The FDA also often inspects one or more sites at which the pivotal clinical trial or trials were conducted to ensure the integrity of the data and compliance with Good Clinical Practice ("GCP"), requirements. If the FDA determines the application, data or manufacturing facilities are not acceptable, the FDA may outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If the FDA evaluation of the NDA and the various inspections are favorable, the FDA may issue an approval letter, which authorizes commercial marketing of the drug with specific prescribing information for a specific indication(s). As a condition of approval of an application, the FDA may request or require post-market testing and surveillance to monitor the drug's safety or efficacy. The FDA also may impose requirements designed to ensure the safety of the drug up to and including distribution and use restrictions under a Risk Evaluation and Mitigation Strategy ("REMS"). After approval, certain changes to the approved product, such as adding new indications, manufacturing changes, or additional labeling claims, are subject to further FDA review and approval before the changes can be implemented. The testing and approval process requires substantial time, effort and financial resources, and we cannot be sure that any approval will be granted on a timely basis, if at all. Product approvals may be further limited or withdrawn if compliance with regulatory standards is not maintained or safety or other problems are identified following initial marketing.

The FDA regulates combinations of products that cross FDA centers, such as drug, biologic or medical device components that are physically, chemically or otherwise combined into a single entity, as a combination product. The FDA center with primary jurisdiction for the combination product will take the lead in the premarket review of the product, with the other center consulting or collaborating with the lead center, and often will require approval of only a single application, such as an NDA. The FDA's Office of Combination Products ("OCP"), determines which center will have primary jurisdiction for the combination product based on the combination product's "primary mode of action." A mode of action is the means by which a product achieves an intended therapeutic effect or action. The primary mode of action is the mode of action that provides the most important therapeutic action of the combination product, or the mode of action expected to make the greatest contribution to the overall intended therapeutic effects of the combination product.

Manufacturing Requirements

After the FDA approves a product, we, our suppliers, and our contract manufacturers must comply with a number of post-approval requirements. For example, holders of an approved NDA are required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with

certain requirements concerning advertising and promotional labeling for their products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP. Accordingly, we and our contract manufacturers must continue to expend time, money, and effort to maintain compliance with cGMP and other aspects of regulatory compliance. In addition, discovery of problems such as safety problems may result in changes in labeling, imposition or modification of a REMS, or other restrictions on a product manufacturer, or NDA holder, including removal of the product from the market.

We use and will continue to use third-party manufacturers to produce our products in clinical and commercial quantities, and we cannot be sure that future FDA inspections will not identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product may result in restrictions on a product, manufacturer, or holder of an approved NDA, including withdrawal of the product from the market. Also, new government requirements may be established that could delay or prevent regulatory approval of our products under development.

Abbreviated New Drug Applications and Section 505(b)(2) New Drug Applications

Once an NDA is approved, the product covered thereby becomes a listed drug that can, in turn, be relied upon by potential competitors in support of approval of an abbreviated new drug application ("ANDA") or 505(b)(2) application. The FDA may approve an ANDA if the product is the same in important respects as the listed drug or if the FDA has declared it suitable for an ANDA submission. In these situations, applicants must submit studies showing that the product is bioequivalent to the listed drug, meaning that the rate and extent of absorption of the drug does not show a significant difference from the rate and extent of absorption of the listed drug. ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Conducting bioequivalence studies is generally less time-consuming and costly than conducting pre-clinical and clinical trials necessary to support an NDA. Drugs approved via ANDAs on the basis that they are the "same" as a listed drug are commonly referred to as "generic equivalents" to the listed drug, and can often be and are substituted by pharmacists under prescriptions written for the original listed drug. For example, a number of ANDAs have been filed and approved with respect to Angiomax. The regulations governing marketing exclusivity and patent protection are complex, and until the outcomes of our effort to extend the patent term and our patent infringement litigation, we may not know the disposition of such ANDA submissions.

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. An ANDA applicant relying upon a listed drug is required to certify to the FDA concerning any patents listed for the listed drug product in the FDA's Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable, or will not be infringed by the new product.

A certification that the proposed generic product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the ANDA applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification notice automatically prevents the FDA from granting final approval to the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA also will not be approved until any applicable non-patent exclusivity period, such as exclusivity for obtaining approval of a new chemical entity, for the referenced product has expired, unless the exclusivity period protects an indication or other aspect of labeling that can be "carved out" of the labeling for the proposed generic product. Federal law provides a period of five years following approval of a drug containing no previously approved active moiety during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph IV challenge to a listed patent, in which case the submission may be made four years following the original product approval. Federal law provides for a period of three years of exclusivity during which the FDA cannot grant effective approval of an ANDA if a listed drug contains a previously approved active moiety but FDA requires as a condition of approval new clinical trials conducted by or for the sponsor. This three-year exclusivity period often protects changes to a previously approved product, such as a new dosage form, route of administration, combination, or indication. Under the Best Pharmaceuticals for Children Act, federal law also provides that periods of patent and non-patent marketing exclusivity listed in the Orange Book for a drug may be extended by six months if the NDA sponsor conducts pediatric studies identified by the FDA in a written request. For written requests issued by the FDA after September 27, 2007, the date of enactment of the Food and Drug Administrative Amendment Act ("FDAAA"), the FDA must grant pediatric exclusivity no later than nine months prior to the date of expiration of patent or non-patent exclusivity in order for the six-month pediatric extension to apply to that exclusivity period.

Most drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on the FDA's previous approval of a similar product, or published literature, in support of its application. 505(b)(2) NDAs often provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) 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. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication(s) sought by the Section 505(b)(2) applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would be required

to do so. As a result, approval of a 505(b)(2) NDA can be prevented until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

U.S. Healthcare Reform

We are continually evaluating the impact of healthcare reform-related programs and regulations on our business. As of the date of this prospectus supplement, we have not identified any provisions that currently materially impact our business and results of operations. However, the potential impact of healthcare reform measures on our business and results of operations is inherently difficult to predict because many of the details regarding the implementation of this legislation have not been determined. In addition, the impact on our business and results of operations may change as and if our business evolves. President Trump and HHS Secretary Azar have announced support for regulatory provisions that would limit a number of healthcare reform programs initiated under the Obama administration, and have proposed or are considering additional reforms. It remains unclear whether these reforms will include similar limitations affecting reimbursement, although scrutiny over drug pricing and government costs is expected to continue. Similarly, efforts in Congress to reform Medicare and Medicaid may impact the pharmaceutical and healthcare industries.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. Sales of inclisiran, if approved, will depend, in part, on the extent to which the costs of the product will be covered by third-party payers, including government health programs such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payer will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payer will pay for the drug product once coverage is approved. Third-party payers may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the approved drugs for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive health economic studies in order to demonstrate the economics of the product, in addition to incurring the costs required to obtain FDA or other comparable regulatory approvals. Even if a drug product is covered, a payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payers are increasingly challenging the prices charged for medical products and services and examining the medical necessity and economic benefit of medical products and services, in addition to their safety and efficacy. If these third-party payers do not consider inclisiran to be economically beneficial compared to other available therapies, they may not cover it after approval as a benefit under their plans. Third-party payers may provide coverage, but place stringent limitations on such coverage, such as requiring alternative treatments to be tried first. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs.

Pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries

may require the completion of additional studies that compare the cost-effectiveness of inclisiran to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drug products will allow favorable reimbursement and pricing arrangements for inclisiran.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payers fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on drug pricing. Coverage policies, third party reimbursement rates and drug pricing regulation may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Foreign Regulations

In addition to regulations in the United States, we are 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 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 much like the IND prior to the commencement of human clinical trials. In Europe, for example, a clinical trial application ("CTA"), must be submitted to each country's national health authority and an independent ethics committee for each clinical trial, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, the clinical trial may proceed in that country.

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 are conducted in accordance with Good Clinical Practices ("GCPs"), and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological product under European Union regulatory systems, we must submit a marketing authorization application. The application used to file the NDA in the United States is similar to that required in Europe, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Drugs can be authorized in the European Union by using either the centralised authorisation procedure or national authorization procedures.

Centralised EMA Procedure. The EMA, formerly the EMEA, implemented the centralised procedure for the approval of human medicines to facilitate marketing authorisations that are valid throughout the European Union. This procedure results in a single marketing authorisation issued by the EMA that is valid across the European Union, as well as Iceland, Liechtenstein and Norway. The centralised procedure is compulsory for human medicines that are derived from biotechnology processes, contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions, and officially designated orphan medicines.

For drugs that do not fall within these categories, an applicant has the option of submitting an application for a centralised marketing authorisation to the EMA, as long as the drug concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.

National Procedures. There are also three other possible routes to authorize medicinal products outside the scope of the centralised procedure and the EMA:

- *National procedures.* A medicine is authorised in one European Union member state in accordance with the national procedures of that country. If a marketing authorisation holder wishes to apply subsequently for additional marketing authorisations in other member states for that product, the mutual recognition procedure must be used.

- *Decentralised procedure.* Using the decentralised procedure, an applicant may apply for simultaneous authorization in more than one European Union country of medicinal products that have not yet been authorized in any European Union country and that do not fall within the mandatory scope of the centralised procedure.

- *Mutual recognition procedure.* In the mutual recognition procedure, a medicine is first authorized in one European Union member state, in accordance with the national procedures of that country, as described above. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

Research and Development

Our research and development expenses, excluding discontinued operations, totaled $133.0 million in 2018, $138.4 million in 2017 and $92.1 million in 2016.

Properties

We lease our principal office in Parsippany, New Jersey, U.S. The lease for Parsippany office covers 173,146 square feet and expires January 2024. We also lease 63,000 square feet of office and laboratory space in San Diego, California. This lease expires in September 2028. On January 11, 2018, we entered into an agreement to sublease 32,039 square feet of the office and laboratory space in San Diego. On August 24, 2018, we entered into an agreement to sublease the remaining office and laboratory space in San Diego. The sublease agreements have terms of 84 months and 48 months, respectively.

We believe that all of our facilities are in good condition and are well maintained and that our current arrangements will be sufficient to meet our needs for the foreseeable future.

Employees

As of February 25, 2019 we employed approximately 62 persons worldwide. We believe that our success depends greatly on our ability to identify, attract and retain capable employees. We have assembled a management team with significant experience in drug development and commercialization. Our employees are not represented by any collective bargaining unit, and we believe our relations with our employees are good.

Workforce Restructuring

In 2017 and 2018, we conducted a series of workforce reductions, as described below and reduced our personnel to less than 60 full time employees. Upon signing release agreements, affected employees have received a severance package, including reduction payments and fully paid health care coverage and outplacement services for six months to a year.

In June 2017, in connection with our voluntary discontinuation and withdrawal of Ionsys from the market in the United States, we commenced a workforce reduction, which resulted in the reduction of 57 employees, which represented approximately 15% of our workforce.

Commencing in December 2017 and continuing through 2018, we implemented a series of workforce reductions to focus on inclisiran, improve efficiencies and better align costs and structure. Through December 31, 2018, 136 employees have been terminated and 136 employees were transferred as part of the sale of the infectious disease business unit to Melinta. These workforce reductions are expected to reduce headcount costs included in operating expenses by approximately $74.0 million on an annualized basis.

Legal Proceedings

From time to time we are party to legal proceedings in the course of our business in addition to those described below. We do not, however, expect such other legal proceedings to have a material adverse effect on our business, financial condition or results of operations.

Melinta and Fortis Litigations

In December 2018, Melinta filed a complaint in the Court of Chancery of the State of Delaware alleging that we breached certain representations and warranties in the purchase and sale agreement pursuant to which Melinta acquired our infectious disease business. In connection with the lawsuit, Melinta is seeking indemnification under the purchase and sale agreement and notified us that it would not be paying the Vabomere Milestone Payment or the first of two $25 million deferred payments due to us under the purchase and sale agreement because Melinta believes it has the right to set-off such payments against its claimed damages in its lawsuit. We have contested Melinta's indemnification and right of set-off assertions. On January 9, 2019, we filed a motion to dismiss Melinta's complaint against us, and on March 15, 2019, we filed our opening brief in support of that motion. On April 23, 2019, Melinta filed an amended complaint containing additional allegations to support their purported claims against us. On May 3, 2019 we filed a motion to dismiss Melinta's amended complaint against us, and on June 10, 2019, we filed our opening brief in support of that motion. Although we believe Melinta's claims are meritless and we will vigorously defend any and all claims brought against us by Melinta and seek full payment by Melinta of its obligations under the purchase and sale agreement, litigation is subject to inherent uncertainty.

On December 28, 2018, we sent a demand letter to Melinta regarding its failure to pay the Vabomere Milestone Payment. On January 7, 2019, we received a letter on behalf of Fortis

Advisors LLC, or Fortis, in its capacity as the representative for the interests of former equity holders of Rempex Pharmaceuticals, Inc. ("Rempex"), demanding that we pay the Vabomere Milestone Payment. On January 28, 2019, we notified Fortis that, while we agree that we are ultimately responsible for the Vabomere Milestone Payment even though it was assumed by Melinta, we believe that we are responsible for such payment only if Fortis is unable to collect from Melinta after exercising due diligence in attempting to collect from Melinta before seeking to collect from us. On March 28, 2019, Fortis filed a complaint in the Court of Chancery of the State of Delaware against Melinta and us regarding the non-payment of the Vabomere Milestone Payment. On April 18, 2019, we filed an answer to Fortis's complaint and a crossclaim against Melinta, alleging breach of contract and requesting that the Court order Melinta to fulfill its obligations under the purchase and sale agreement, including complying with payment obligations in connection with the Vabomere Milestone Payment, among other relief. That same day, Melinta filed a motion to dismiss Fortis's complaint, and filed its opening brief in support of that motion on May 31, 2019. On May 8, 2019, Melinta filed its answer to our crossclaim. On May 20, 2019, Fortis filed both a motion for partial judgment on the pleadings against us and its brief in support of that motion. On June 21, 2019, we filed both our motion for judgment on the pleadings against Melinta and our combined answering and opening brief, which both opposed Fortis's motion for partial judgment on the pleadings and supported our affirmative motion for judgment on the pleadings against Melinta. Oral argument on Fortis's Motion for Partial Judgment on the Pleadings is currently scheduled for September 19, 2019. Although we will vigorously contest Fortis's claims on the basis they must first exercise due diligence in attempting to collect the Vabomere Milestone Payment from Melinta before they seek to collect from us, litigation is subject to inherent uncertainty.

SymBio Arbitration

On October 11, 2017, SymBio Pharmaceuticals Limited ("SymBio"), filed a Request for Arbitration with the International Chamber of Commerce's International Court of Arbitration against us and our wholly owned subsidiary, Incline Therapeutics, Inc. ("Incline"). In the Request for Arbitration, SymBio claims that we failed to provide adequate assurances of performance of, or, alternatively, have rendered ourselves unable to perform, our obligations under the license agreement between us, Incline and SymBio relating to the development and commercialization of Ionsys in Japan. As a result, SymBio seeks compensatory damages in an amount of $82 million. On December 15, 2017, we filed an Answer and Counterclaim denying SymBio's allegations, asserting defenses to SymBio's claims, and bringing a counterclaim for breach of contract. We are seeking compensatory damages in an amount of $10 million. The arbitration process is ongoing. We intend to defend ourselves vigorously in this matter and pursue all relief to which we are entitled.

Silence Therapeutics Litigation

In October 2017, Silence served a claim in the High Court of Justice, Chancery Division, Patents Court in the United Kingdom, naming The Medicines Company UK Ltd., our wholly owned subsidiary, Alnylam and Alnylam UK Limited, as co-defendants. In Silence's claim, it sought a determination that it is entitled to SPCs based on its '847 patent and the prospective European regulatory approvals for inclisiran and for certain of Alnylam's product candidates. This was based on Silence's assertion that inclisiran and the cited Alnylam product candidates fall within the scope of the '847 patent. An SPC is an intellectual property right that could extend the life of the Silence patent in relation to a specified product for a period of up to five additional years bringing the expiration date up to 2028. In addition, Silence sought costs, interest and other unspecified relief. On October 31, 2017, we acknowledged service of the claim served by Silence and on November 30, 2017, submitted substantive defenses to the claim.

On October 27, 2017, we and Alnylam filed and served a claim against Silence in the High Court seeking revocation of the '847 patent, as well as a declaration of non-infringement by inclisiran and

certain of Alnylam's product candidates of the '847 patent, and costs and interest among other potential remedies. On November 14, 2017, Silence filed a defense to our claim along with counterclaims alleging infringement of the '847 patent by inclisiran and certain of Alnylam's product candidates. On December 11, 2017, we filed an answer and defense to the counterclaims.

The High Court had listed the trial for 10 days which was to be heard in a window starting on December 3, 2018 for all claims between Silence, Alnylam and us. However, on June 29, 2018, Silence withdrew the proceedings it issued against us seeking a determination that it is entitled to SPCs based on the '847 patent and the prospective European regulatory approvals for inclisiran. In the remaining revocation and infringement proceedings based on the '847 patent, on July 2, 2018, Silence filed an application for an order for permission to amend the '847 patent. At the same time Silence confirmed to us that it will no longer assert that inclisiran falls within the scope of the '847 patent in the UK. In light of these developments, a UK Court Order was issued by which the Court declared that no act done in the UK with respect to inclisiran would infringe the '847 patent. Silence was also ordered to pay our legal costs in defending Silence's claim and our costs in commencing the revocation action in response. The trial between Silence and Alnylam was scheduled to continue without us and to be heard in December 2018.

In parallel to the above High Court proceedings, on December 14, 2017 we also commenced opposition proceedings at the EPO seeking revocation of the '847 patent. Alnylam and Sanofi also each commenced opposition proceedings for the revocation of the '847 patent at the EPO. Also, on October 16, 2018 we commenced opposition proceedings at the EPO seeking revocation of European Patent No. 1,857,547 ("547 patent"), which was recently granted by the EPO to Silence and is in the same patent family as the '847 patent.

On December 9, 2018, Silence and Alnylam entered into a settlement and license agreement pursuant to which Alnylam received a global license to Silence's relevant intellectual property for all current and future Alnylam products, including inclisiran, for a low royalty on Alnylam's ONPATTRO product in the European Union through 2023. The settlement does not contain any milestones or royalty payments due to Silence with respect to inclisiran. In connection with the settlement, we entered into an agreement with Alnylam and Silence to discontinue all of our pending litigation against Silence and EPO oppositions of Silence's patents, and we agreed to forgo any reimbursement of legal costs from Silence. Under our collaboration agreement with Alnylam, we received a license from Alnylam covering the license rights granted to Alnylam from Silence with no additional milestone payments or royalties.

On February 15, 2019, in accordance with the terms of the agreement with Alnylam and Silence, we withdrew from the opposition proceedings at the EPO in respect of both the '847 patent and the '547 patent. As a result there are no ongoing proceedings in the United Kingdom, at the EPO or elsewhere in Europe between us and Silence.

Biogen Idec Litigation

On September 15, 2015, Biogen Idec ("Biogen") notified us that after completing an audit of our books and records for the fourth quarter of 2014, Biogen believed it was owed additional royalties relating to Angiomax under our license agreement with Biogen. On September 23, 2015, we filed suit against Biogen in the United States District Court for the District of New Jersey seeking, *inter alia*, declaratory judgments that we have satisfied our obligations under the license agreement. On November 12, 2015, Biogen answered the complaint denying our claims and asserting counterclaims for breach of contract. In February 2017, Biogen's claim for audit costs was voluntarily dismissed. Following settlement discussions, the parties agreed to settle the case and entered into a joint stipulation and order of dismissal with prejudice. As part of the settlement, we made an upfront payment of $1.2 million upon entering into the settlement agreement and agreed to make additional payments of $4 million, in the aggregate, on June 30, 2020 and June 30, 2021.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS

The following is a discussion of material U.S. federal income tax considerations applicable to Non-U.S. Holders (as defined below) with respect to the ownership and disposition of our common stock issued pursuant to this offering. The following discussion is based upon current provisions of the Internal Revenue Code of 1986, as amended (the "Code"), U.S. judicial decisions, administrative pronouncements and existing Treasury regulations, all as in effect as of the date hereof. All of the preceding authorities are subject to change at any time, possibly with retroactive effect, so as to result in U.S. federal income tax consequences different from those discussed below. We have not requested, and will not request, a ruling from the U.S. Internal Revenue Service (the "IRS") with respect to any of the U.S. federal income tax consequences described below, and as a result there can be no assurance that the IRS will not disagree with or challenge any of the conclusions we have reached and describe herein.

This discussion only addresses beneficial owners of our common stock that hold such common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all aspects of U.S. federal income taxation that may be important to a Non-U.S. Holder in light of such Non-U.S. Holder's particular circumstances or that may be applicable to Non-U.S. Holders subject to special treatment under U.S. federal income tax law (including, for example, financial institutions, regulated investment companies, real estate investment trusts, dealers in securities, traders in securities that elect mark-to-market treatment, insurance companies, tax-exempt entities, Non-U.S. Holders who acquire our common stock pursuant to the exercise of employee stock options or otherwise as compensation for their services, controlled foreign corporations, passive foreign investment companies, former citizens or former long-term residents of the United States, and Non-U.S. Holders that hold our common stock as part of a straddle, constructive sale or conversion transaction). In addition, this discussion does not address U.S. federal tax laws other than those pertaining to the U.S. federal income tax (such as U.S. federal estate, the alternative minimum tax or gift tax or the Medicare contribution tax on certain net investment income), nor does it address any aspects of U.S. state, local or non-U.S. taxes. Non-U.S. Holders are urged to consult their own tax advisors regarding the possible application of these taxes.

For the purposes of this discussion, the term "Non-U.S. Holder" means a beneficial owner of our common stock that is an individual, corporation, estate or trust, other than:

- an individual who is a citizen or resident of the United States, as determined for U.S. federal income tax purposes;
- a corporation, or other entity taxable as a corporation for U.S. federal income tax purposes, created or organized in the United States or under the laws of the United States, any state thereof or the District of Columbia;
- an estate, the income of which is includible in gross income for U.S. federal income tax purposes regardless of its source; or
- a trust if: (i) a court within the United States is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have the authority to control all substantial decisions of the trust; or (ii) it has a valid election in effect under applicable U.S. Treasury regulations to be treated as a domestic trust.

If an entity or arrangement treated as a partnership for U.S. federal income tax purposes holds shares of our common stock, the tax treatment of a person treated as a partner of such partnership generally will depend on the status of the partner and the activities of the partnership. Persons that, for U.S. federal income tax purposes, are treated as partners in a partnership holding shares of our common stock are urged to consult their own tax advisors.

Prospective purchasers are urged to consult their tax advisors as to the particular consequences to them under U.S. federal, state and local, and applicable non-U.S. tax laws of the acquisition, ownership and disposition of our common stock.

Distributions

Although we do not anticipate that we will make any distributions on our common stock in the foreseeable future, distributions of cash or property that we pay in respect of our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Subject to the discussions below under "—U.S. Trade or Business Income," "—Information Reporting and Backup Withholding" and "—FATCA," you generally will be subject to U.S. federal withholding tax at a 30% rate, or at a reduced rate prescribed by an applicable income tax treaty, on any dividends received in respect of our common stock. If the amount of the distribution exceeds our current and accumulated earnings and profits, such excess first will be treated as a return of capital to the extent of your tax basis in our common stock, and thereafter will be treated as capital gain. However, except to the extent that the intermediary through which you hold your common stock elects otherwise, the intermediary must generally withhold on the entire distribution, in which case you will be entitled to a refund from the IRS for the withholding tax on any portion of the distribution that exceeds our current and accumulated earnings and profits.

In order to obtain a reduced rate of U.S. federal withholding tax under an applicable income tax treaty, you will be required to provide a properly executed IRS Form W-8BEN or Form W-8BEN-E (or, in each case, a successor form) certifying your entitlement to benefits under the treaty. If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, you may obtain a refund or credit of any excess amounts withheld by filing an appropriate claim for a refund with the IRS. You are urged to consult your own tax advisor regarding your possible entitlement to benefits under an applicable income tax treaty.

Sale, Exchange or Other Taxable Disposition of Common Stock

Subject to the discussions below under "—U.S. Trade or Business Income," "—Information Reporting and Backup Withholding" and "—FATCA," you generally will not be subject to U.S. federal income or withholding tax in respect of any gain on a sale, exchange or other taxable disposition of our common stock unless:

- the gain is U.S. trade or business income, in which case, such gain will be taxed as described in "—U.S. Trade or Business Income" below;
- you are an individual who is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met, in which case you will be subject to U.S. federal income tax at a rate of 30% (or a reduced rate under an applicable income tax treaty) on the amount by which certain capital gains allocable to U.S. sources exceed certain capital losses allocable to U.S. sources; or
- we are or have been a "United States real property holding corporation" (a "USRPHC") under Section 897 of the Code at any time during the shorter of the five-year period ending on the date of the disposition and your holding period for the common stock, in which case, subject to the exception set forth in the third sentence of the next paragraph, such gain will be subject to U.S. federal income tax in the same manner as U.S. trade or business income discussed below.

In general, a corporation is a USRPHC if the fair market value of its "United States real property interests" equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests and its other assets used or held for use in a trade or business. If we were determined to be a

USRPHC, gain would not be subject to tax as U.S. trade or business income if your holdings (direct and indirect) at all times during the applicable period described in the third bullet point above constituted 5% or less of our common stock, provided that our common stock was regularly traded on an established securities market during such period. We believe that we are not currently, and we do not anticipate becoming in the future, a "United States real property holding corporation" for U.S. federal income tax purposes.

U.S. Trade or Business Income

For purposes of this discussion, dividend income and gain on the sale, exchange or other taxable disposition of our common stock will be considered to be "U.S. trade or business income" if (A)(i) such income or gain is effectively connected with your conduct of a trade or business within the United States and (ii) if you are eligible for the benefits of an income tax treaty with the United States and such treaty requires, such gain is attributable to a permanent establishment (or, if you are an individual, a fixed base) that you maintain in the United States or (B) with respect to gain, we are or have been a USRPHC at any time during the shorter of the five-year period ending on the date of the disposition of our common stock and your holding period for our common stock (subject to the 5% ownership exception set forth above in the second paragraph of "—Sale, Exchange or Other Taxable Disposition of Common Stock)." Generally, U.S. trade or business income is not subject to U.S. federal withholding tax (provided that you comply with applicable certification and disclosure requirements, including providing a properly executed IRS Form W-8ECI (or successor form)); instead, you are subject to U.S. federal income tax on a net basis at regular U.S. federal income tax rates (generally in the same manner as a U.S. person) on your U.S. trade or business income. If you are a corporation, any U.S. trade or business income that you receive may also be subject to a "branch profits tax" at a 30% rate, or at a lower rate prescribed by an applicable income tax treaty.

Information Reporting and Backup Withholding

Any dividend income that is subject to U.S. federal withholding tax or that is exempt from such withholding pursuant to an income tax treaty will be reported to the IRS and to each Non-U.S. Holder. Copies of these information returns may also be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which a Non-U.S. Holder resides. Under certain circumstances, the Code imposes a backup withholding obligation on certain reportable payments. Dividends paid to you will generally be exempt from backup withholding if you provide a properly executed IRS Form W-8BEN or Form W-8BEN-E (or, in each case, a successor form) or otherwise establish an exemption and the payor does not have actual knowledge or reason to know that you are a U.S. person or that the conditions of such other exemption are not, in fact, satisfied.

The payment of the proceeds from the disposition of our common stock to or through the U.S. office of any broker (U.S. or non-U.S.) will be subject to information reporting and possible backup withholding unless you certify as to your non-U.S. status under penalties of perjury or otherwise establish an exemption and the broker does not have actual knowledge or reason to know that you are a U.S. person or that the conditions of any other exemption are not, in fact, satisfied. The payment of proceeds from the disposition of our common stock to or through a non-U.S. office of a non-U.S. broker will not be subject to information reporting or backup withholding unless the non-U.S. broker has certain types of relationships with the United States (a "U.S. related financial intermediary"). In the case of the payment of proceeds from the disposition of our common stock to or through a non-U.S. office of a broker that is either a U.S. person or a U.S.-related financial intermediary, the Treasury regulations require information reporting (but not backup withholding) on the payment unless the broker has documentary evidence in its files that the owner is not a U.S. person and the broker has no knowledge to the contrary. You are urged to consult your tax advisor on the application of information reporting and backup withholding in light of your particular circumstances.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to you will be refunded or credited against your U.S. federal income tax liability, if any, provided that the required information is timely furnished to the IRS.

FATCA

Pursuant to Section 1471 through 1474 of the Code, commonly referred to as the Foreign Account Tax Compliance Act ("FATCA"), foreign financial institutions (which include most foreign hedge funds, private equity funds, mutual funds, securitization vehicles and any other investment vehicles) and certain other foreign entities that do not otherwise qualify for an exemption must comply with information reporting rules with respect to their U.S. account holders and investors or be subject to a withholding tax on U.S. source payments made to them (whether received as a beneficial owner or as an intermediary for another party).

More specifically, a foreign financial institution or other foreign entity that does not comply with the FATCA reporting requirements or otherwise qualify for an exemption will generally be subject to a 30% withholding tax with respect to any "withholdable payments." For this purpose, withholdable payments generally include U.S.-source payments otherwise subject to nonresident withholding tax (e.g., U.S.-source dividends). Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

FATCA currently applies to any dividends made in respect of our common stock. Pursuant to recently proposed Treasury regulations, FATCA withholding would not apply to gross proceeds from dispositions of U.S. common stock. To avoid withholding on dividends, Non-U.S. Holders may be required to provide the Company (or its withholding agents) with applicable tax forms or other information. Non-U.S. Holders are urged to consult with their own tax advisors regarding the effect, if any, of the FATCA provisions to them based on their particular circumstances.

UNDERWRITING

The Company and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman Sachs & Co. LLC and J.P. Morgan Securities LLC are the representatives of the underwriters.

Underwriters	Number of Shares
Goldman Sachs & Co. LLC	
J.P. Morgan Securities LLC	
Total	

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

If the underwriters sell more shares than the total number set forth in the table above, the underwriters have an option to buy up to an additional shares from the Company. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

Paid by the Company	No Exercise	Full Exercise
Per Share	$	$
Total	$	$

Shares sold by the underwriters to the public will initially be offered at the initial price to public set forth on the cover of this prospectus. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $ per share from the initial public offering price. If all the shares are not sold at the initial public offering price, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

We have agreed that we will not, without the prior written consent of Goldman Sachs & Co. LLC and J.P. Morgan Securities LLC on behalf of the underwriters, for a period of 90 days after the date of this prospectus supplement:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any shares of our common stock or any securities convertible into or exercisable or exchangeable for common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing; or

- enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or any such other securities, whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise.

The restrictions described above do not apply to:

- the shares to be sold in the offering;
- any shares of our common stock issued upon the exercise of options granted under our company stock plans in effect as of the date of this prospectus supplement or upon the vesting of restricted stock units and performance share awards and warrants described as outstanding in this prospectus supplement;
- any options and other awards granted under our company stock plans in effect on the date of this prospectus supplement or the grant of common stock under an employee stock purchase plan in effect on the date of this prospectus supplement; or
- the issuance of our common stock or other securities in connection with any strategic transaction involving a commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements); or the issuance of our common stock or other securities in connection with any strategic transaction involving any acquisition of assets of not less than a majority or controlling portion of the equity of another entity; provided that the amount of shares to be received by any such third party pursuant to this bullet is less than 5% of the outstanding shares of our common stock, and any such shares of our common stock and securities issued pursuant to this bullet during the 90-day period shall be subject to the restrictions described above for the remainder of the 90-day period.

Our directors and our executive officers have agreed that they will not, without the prior written consent of Goldman Sachs & Co. LLC and J.P. Morgan Securities LLC, on behalf of the underwriters, for a period of 90 days after the date of this prospectus supplement:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock, or any securities convertible into or exercisable or exchangeable for common stock (including without limitation, common stock or such other securities which may be deemed to be beneficially owned by such person in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), or publicly disclose the intention to make any offer, sale, pledge or disposition;
- enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities; or
- make any demand for or exercise any right with respect to the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock, whether any such transaction described in the first two bullet points above is to be settled by delivery of common stock or such other securities, in cash or otherwise.

None of the restrictions imposed in the lock-up agreement to be entered into by Alexander Denner will apply in any manner, directly or indirectly, to Sarissa Capital Management LP, Sarissa Capital Domestic Fund LP, Sarissa Capital Offshore Master Fund LP, or any related entities or to any securities held or actions taken (or not taken) by any of the foregoing.

With respect to our directors and executive officers, the restrictions described above do not apply, subject to certain conditions, to the transfer or disposition of shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock:

- as a bona fide gift or gifts;
- to the immediate family of such person;

- to any trust for the direct or indirect benefit of such person or the immediate family of such person in a transaction not involving a disposition for value;

- to any corporation, partnership, limited liability company or other entity all of the beneficial ownership interests of which are held by such person or the immediate family of such person in a transaction not involving a disposition for value;

- by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the undersigned; or

- to a bona fide third party pursuant to a tender or exchange offer or any other transaction, including, without limitation, a merger, consolidation or other business combination involving a change in control of our company, that, in each case, has been approved by our board of directors (including, without limitation, entering into any lock-up, voting or similar agreement pursuant to which the securityholder may agree to transfer, sell, tender or otherwise dispose of the securityholder's securities in connection with any such transaction, or vote any of the securityholder's securities in favor of any such transaction), provided that all of the securities not so transferred, sold, tendered or otherwise disposed of remain subject to the lock-up agreement and also provided that as a condition of such transfer, sale, tender or other disposition, if such tender offer or other transaction is not completed, such securities will remain subject to the lock-up restrictions.

Furthermore, notwithstanding the restrictions described above, such director or executive officer may, subject to certain conditions:

- exercise an option or warrant to purchase shares of our common stock;

- effect transactions pursuant to a trading plan established pursuant to Rule 10b5-1 under the Exchange Act in existence as of the date of this prospectus supplement; and

- establish a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of our common stock, provided that such plan does not provide for any transfers of our common stock during the 90-day period.

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Shorts sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares from the Company in the offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option granted to them. "Naked" short sales are any sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the Company's stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued at any time. These transactions may be effected on NASDAQ, in the over-the-counter market or otherwise.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our common stock on The Nasdaq Global Select Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The Nasdaq Global Select Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

The Company may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. In connection with those derivatives, the third parties may sell securities covered by this prospectus, including in short sale transactions. If so, the third party may use securities pledged by the Company or borrowed from the Company or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from the Company in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter or will be identified in a post-effective amendment.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

Selling Restrictions

Canada

The shares of our common stock may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus 156 Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares of our common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws. Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment

thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor. Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

United Kingdom

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, or FSMA), received by it in connection with the issue or sale of our Class A common shares in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(a) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to our Class A common shares in, from or otherwise involving the United Kingdom.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), each underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date) it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the representatives of the underwriters for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of our common shares shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer of shares to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

Each underwriter has represented and agreed that:

(b) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) received by it in connection with the issue or sale of the shares in circumstances in which Section 21(1) of the FSMA would not apply to the Issuer; and

(c) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Japan

The shares have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose

is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Singapore Securities and Futures Act Product Classification: Solely for the purposes of its obligations pursuant to Sections 309B(1) (a) and 309B(1)(c) of the SFA, we have determined, and hereby notify all relevant persons (as defined in Section 309A of the SFA) that the common units are "prescribed capital markets products" (as defined in the Securities and Futures (Capital Markets Products) Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04- N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

The Company estimates that its share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately $.

The Company has agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for the issuer, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments of the issuer. The underwriters and their respective affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Paul, Weiss, Rifkind, Wharton & Garrison LLP. The underwriters are being represented in connection with this offering by Davis Polk & Wardwell LLP.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2018, and the effectiveness of our internal control over financial reporting as of December 31, 2018, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements and our management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2018 are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at http://www.themedicinescompany.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus.

This prospectus supplement is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus supplement and the accompanying prospectus regarding us and the securities, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's internet site.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference in this prospectus supplement and the accompanying prospectus much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement and the accompanying prospectus is considered to be part of this prospectus supplement and the accompanying prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement and the accompanying prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement and the accompanying prospectus incorporate by reference the documents listed below (File No. 000-31191) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the registration statement is terminated or completed:

- Our Annual Report on Form 10-K for the fiscal year ended December 31, 2018 (filed on February 27, 2019) , including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2019 Annual Meeting of Stockholders ;
- Our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2019 (filed on April 26, 2019);
- Our Current Reports on Form 8-K filed on January 4, 2019; January 14, 2019; March 18, 2019; and June 5, 2019; and
- The description of our common stock contained in our Registration Statement on Form 8-A filed on July 28, 2000, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or phone number:

The Medicines Company
8 Sylvan Way
Parsippany, New Jersey 07054
Attn: Investor Relations
Phone: (973) 290-6000

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PROSPECTUS

The Medicines Company

Debt Securities
Common Stock
Preferred Stock
Depositary Shares
Purchase Contracts
Purchase Units
Warrants

We may issue securities from time to time in one or more offerings. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any applicable prospectus supplement before you invest.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement.

Our common stock trades on The NASDAQ Global Select Market under the symbol "MDCO."

Investing in these securities involves significant risks. See "Risk Factors" beginning on page 2 of this prospectus and the "Risk Factors" section included in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase these securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is June 24, 2019

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading "Where You Can Find More Information" beginning on page 4 of this prospectus.

We have not authorized anyone to provide you with information different from that contained in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We do not take any responsibility for, and cannot provide any assurance as to the reliability of, any information other than the information in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to "we," "our," "us" and "the Company" refer, collectively, to The Medicines Company, a Delaware corporation, and its consolidated subsidiaries.

RISK FACTORS

Investing in our securities involves significant risks. You should carefully consider the risks and uncertainties described in this prospectus and any accompanying prospectus supplement, including the risk factors set forth in our filings with the SEC that are incorporated by reference herein, including the risk factors in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018 and our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2019, before making an investment decision pursuant to this prospectus and any accompanying prospectus supplement relating to a specific offering. Our business, financial condition and results of operations could be materially and adversely affected by any or all of these risks or by additional risks and uncertainties not presently known to us or that we currently deem immaterial that may adversely affect us in the future.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at http://www.themedicinescompany.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus.

This prospectus is part of a registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference in this prospectus much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 000-31191) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the registration statement is terminated or completed:

- Our Annual Report on Form 10-K for the fiscal year ended December 31, 2018 (filed on February 27, 2019) , including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2019 Annual Meeting of Stockholders ;
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You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or phone number:

The Medicines Company
8 Sylvan Way
Parsippany, New Jersey 07054
Attn: Investor Relations
Phone: (973) 290-6000

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference in this prospectus include "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Exchange Act. All statements contained or incorporated by reference herein regarding our company, the securities offered hereby, any offering contemplated by this prospectus, our strategy, future operations, financial position, future revenue, projected costs, prospects, plans and objectives of management, other than statements of historical facts, are forward-looking statements. The words "anticipates," "believes," "estimates," "expects," "intends," "may," "plans," "projects," "will," "would" and similar expressions are intended to identify forward looking statements, although not all forward looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations expressed or implied in our forward looking statements. There are a number of important factors that could cause actual results, levels of activity, performance or events to differ materially from those expressed or implied in the forward looking statements we make. These important factors include our "critical accounting estimates" described in Part II, Item 7 "Management's Discussion and Analysis of Financial Condition and Results of Operations —Application of Critical Accounting Estimates" of our Annual Report on Form 10-K for the fiscal year ended December 31, 2018 and Part I, Item 2 of our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2019, each of which is incorporated herein by reference; and the factors set forth under the caption "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018 and our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2019, each of which is incorporated herein by reference, and beginning on page 4 of this prospectus.

THE MEDICINES COMPANY

We are a biopharmaceutical company driven by our purpose solve major medical, societal and economic challenges in healthcare. We have a singular focus on one of the greatest global healthcare challenges and burdens—that presented by atherosclerotic cardiovascular disease, or ASCVD, which remains the number one cause of death in the United States and worldwide. We take on that challenge by developing inclisiran, the investigational RNA interference, or RNAi, therapeutic, that specifically inhibits production of proprotein convertase subtilisin/kexin type 9, or PCSK9, a key protein that controls LDL-cholesterol, or LDL-C, levels. We believe inclisiran is uniquely suited to make a significant difference reducing risk in ASCVD. We have the right to develop, manufacture and commercialize inclisiran under our collaboration agreement with Alnylam Pharmaceuticals, Inc., or Alnylam.

Our principal executive offices are located at 8 Sylvan Way, Parsippany, New Jersey 07054, and our telephone number is (973) 290-6000.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus to fund our development of inclisiran and for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include the acquisition of complementary products, technologies or businesses, repayment and refinancing of debt, working capital and capital expenditures. We may temporarily invest the net proceeds in investment-grade, interest-bearing securities until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior or subordinated. We refer to the senior debt securities and the subordinated debt securities collectively as debt securities. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered. When we refer to "the Company," "we," "our," and "us" in this section, we mean The Medicines Company excluding, unless the context otherwise requires or as otherwise expressly stated, our subsidiaries.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. Together, the senior indenture and the subordinated indenture are referred to as the indentures and, together, the senior trustee and the subordinated trustee are referred to as the trustees. This prospectus briefly outlines some of the provisions of the indentures. The following summary of the material provisions of the indentures is qualified in its entirety by the provisions of the indentures, including definitions of certain terms used in the indentures. Wherever we refer to particular sections or defined terms of the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information.

None of the indentures will limit the amount of debt securities that we may issue. The applicable indenture will provide that debt securities may be issued up to an aggregate principal amount authorized from time to time by us and may be payable in any currency or currency unit designated by us or in amounts determined by reference to an index.

General

The senior debt securities will constitute our unsecured and unsubordinated general obligations and will rank pari passu with our other unsecured and unsubordinated obligations. The subordinated debt securities will constitute our unsecured and subordinated general obligations and will be junior in right of payment to our senior indebtedness (including senior debt securities), as described under the heading "—Certain Terms of the Subordinated Debt Securities—Subordination."

The debt securities will be our unsecured obligations. Any secured debt or other secured obligations will be effectively senior to the debt securities to the extent of the value of the assets securing such debt or other obligations.

The applicable prospectus supplement and any free writing prospectus will include any additional or different terms of the debt securities being offered, including the following terms:

- the title and type of the debt securities;
- whether the debt securities will be senior or subordinated debt securities, and, with respect to debt securities issued under the subordinated indenture the terms on which they are subordinated;
- the aggregate principal amount of the debt securities;
- the price or prices at which we will sell the debt securities;

- if other than denominations of $2,000 and any integral multiples of $1,000, the denominations in which any debt securities will be issued;
- the maturity date or dates of the debt securities and the right, if any, to extend such date or dates;
- the rate or rates, if any, per year, at which the debt securities will bear interest, or the method of determining such rate or rates;
- the date or dates from which such interest will accrue, the interest payment dates on which such interest will be payable or the manner of determination of such interest payment dates and the related record dates;
- the right, if any, to extend the interest payment periods and the duration of that extension;
- the manner of paying principal and interest and the place or places where principal and interest will be payable;
- the terms of any mandatory redemption or provisions for a sinking fund, purchase fund or other analogous fund, if any;
- any redemption dates, prices, obligations and restrictions on the debt securities;
- the currency, currencies or currency units in which the debt securities will be denominated and the currency, currencies or currency units in which principal and interest, if any, on the debt securities may be payable;
- any conversion or exchange features of the debt securities;
- whether and upon what terms the debt securities may be defeased or discharged;
- any events of default or covenants in addition to or in lieu of those set forth in the indenture;
- whether the debt securities will be issued in definitive or global form or in definitive form only upon satisfaction of certain conditions;
- whether the series of debt securities will be guaranteed as to payment or performance; and
- any other material terms of the debt securities.

The applicable prospectus supplement will also describe any applicable material U.S. federal income tax consequences.

When we refer to "principal" in this section with reference to the debt securities, we are also referring to "premium, if any."

We may from time to time, without notice to or the consent of the holders of any series of debt securities, create and issue further debt securities of any such series ranking equally with the debt securities of such series in all respects (or in all respects other than (1) the payment of interest accruing prior to the issue date of such further debt securities or (2) the first payment of interest following the issue date of such further debt securities). Such further debt securities may be consolidated and form a single series with the debt securities of such series and have the same terms as to status, redemption or otherwise as the debt securities of such series.

You may present debt securities for exchange and you may present debt securities for transfer in the manner, at the places and subject to the restrictions set forth in the debt securities and the applicable prospectus supplement. We will provide you those services without charge, although you may have to pay any tax or other governmental charge payable in connection with any exchange or transfer, as set forth in the indenture.

Debt securities may bear interest at a fixed rate or a floating rate. Debt securities bearing no interest or interest at a rate that at the time of issuance is below the prevailing market rate (original issue discount securities) may be sold at a discount below their stated principal amount.

We may issue debt securities with the principal amount payable on any principal payment date, or the amount of interest payable on any interest payment date, to be determined by reference to one or more currency exchange rates, securities or baskets of securities, commodity prices or indices. You may receive a payment of principal on any principal payment date, or a payment of interest on any interest payment date, that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending on the value on such dates of the applicable currency, security or basket of securities, commodity or index. Information as to the methods for determining the amount of principal or interest payable on any date, the currencies, securities or baskets of securities, commodities or indices to which the amount payable on such date is linked.

Certain Terms of the Senior Debt Securities

Covenants. Unless we indicate otherwise in a prospectus supplement, the senior debt securities will not contain any financial or restrictive covenants, including covenants restricting either us or any of our subsidiaries from incurring, issuing, assuming or guaranteeing any indebtedness secured by a lien on any of our or our subsidiaries' property or capital stock, or restricting either us or any of our subsidiaries from entering into sale and leaseback transactions.

Consolidation, Merger and Sale of Assets. Unless we indicate otherwise in a prospectus supplement, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to any person, in either case, unless:

- the successor entity, if any, is a U.S. corporation or entity (subject to certain exceptions provided for in the senior indenture);
- the successor entity assumes our obligations on the senior debt securities and under the senior indenture;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- certain other conditions are met.

No Protection in the Event of a Change in Control. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any provisions that may afford holders of the senior debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

Events of Default. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the following are events of default under the senior indenture for any series of senior debt securities:

- failure to pay interest on any senior debt securities of such series when due and payable, if that default continues for a period of 90 days (or such other period as may be specified for such series);
- failure to pay principal on the senior debt securities of such series when due and payable whether at maturity, upon redemption, by declaration or otherwise (and, if specified for such series, the continuance of such failure for a specified period);

- default in the performance of or breach of any of our covenants or agreements in the senior indenture applicable to senior debt securities of such series, other than a covenant breach which is specifically dealt with elsewhere in the senior indenture, and that default or breach continues for a period of 90 days after we receive written notice from the trustee or from the holders of 25% or more in aggregate principal amount of the senior debt securities of such series;

- certain events of bankruptcy or insolvency, whether or not voluntary; and

- any other event of default provided for in such series of senior debt securities as may be specified in the applicable prospectus supplement.

Unless we indicate otherwise in a prospectus supplement, the default by us under any other debt, including any other series of debt securities, is not a default under the senior indenture.

If an event of default other than an event of default specified in the fourth bullet point above occurs with respect to a series of senior debt securities and is continuing under the senior indenture, then, and in each such case, either the trustee or the holders of not less than 25% in aggregate principal amount of such series then outstanding under the senior indenture (each such series voting as a separate class) by written notice to us and to the trustee, if such notice is given by the holders, may, and the trustee at the request of such holders shall, declare the principal amount of and accrued interest on such series of senior debt securities to be immediately due and payable, and upon this declaration, the same shall become immediately due and payable.

If an event of default specified in the fourth bullet point above occurs with respect to us and is continuing, the entire principal amount of and accrued interest, if any, on each series of senior debt securities then outstanding shall become immediately due and payable.

Unless otherwise specified in the prospectus supplement relating to a series of senior debt securities originally issued at a discount, the amount due upon acceleration shall include only the original issue price of the senior debt securities, the amount of original issue discount accrued to the date of acceleration and accrued interest, if any.

Upon certain conditions, declarations of acceleration may be rescinded and annulled and past defaults may be waived by the holders of a majority in aggregate principal amount of all the senior debt securities of such series affected by the default, each series voting as a separate class. Furthermore, prior to a declaration of acceleration and subject to various provisions in the senior indenture, the holders of a majority in aggregate principal amount of a series of senior debt securities, by notice to the trustee, may waive an existing default or event of default with respect to such senior debt securities and its consequences, except a default in the payment of principal of or interest on such senior debt securities or in respect of a covenant or provision of the senior indenture which cannot be modified or amended without the consent of the holders of each such senior debt security. Upon any such waiver, such default shall cease to exist, and any event of default with respect to such senior debt securities shall be deemed to have been cured, for every purpose of the senior indenture; but no such waiver shall extend to any subsequent or other default or event of default or impair any right consequent thereto. For information as to the waiver of defaults, see "—Modification and Waiver."

The holders of a majority in aggregate principal amount of a series of senior debt securities may direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to such senior debt securities. However, the trustee may refuse to follow any direction that conflicts with law or the senior indenture, that may involve the trustee in personal liability or that the trustee determines in good faith may be unduly prejudicial to the rights of holders of such series of senior debt securities not joining in the giving of such direction and may take any other action it deems proper that is not inconsistent with any

such direction received from holders of such series of senior debt securities. A holder may not pursue any remedy with respect to the senior indenture or any series of senior debt securities unless:

- the holder gives the trustee written notice of a continuing event of default;
- the holders of at least 25% in aggregate principal amount of such series of senior debt securities make a written request to the trustee to pursue the remedy in respect of such event of default;
- the requesting holder or holders offer the trustee indemnity satisfactory to the trustee against any costs, liability or expense;
- the trustee does not comply with the request within 60 days after receipt of the request and the offer of indemnity; and
- during such 60-day period, the holders of a majority in aggregate principal amount of such series of senior debt securities do not give the trustee a direction that is inconsistent with the request.

These limitations, however, do not apply to the right of any holder of a senior debt security to receive payment of the principal of and interest, if any, on such senior debt security in accordance with the terms of such debt security, or to bring suit for the enforcement of any such payment in accordance with the terms of such debt security, on or after the due date for the senior debt securities, which right shall not be impaired or affected without the consent of the holder.

The senior indenture requires certain of our officers to certify, on or before a fixed date in each year in which any senior debt security is outstanding, as to their knowledge of our compliance with all covenants, agreements and conditions under the senior indenture.

Satisfaction and Discharge. We can satisfy and discharge our obligations to holders of any series of senior debt securities if:

- we pay or cause to be paid, as and when due and payable, the principal of and any interest on all senior debt securities of such series outstanding under the senior indenture; or
- all senior debt securities of such series have become due and payable or will become due and payable within one year (or are to be called for redemption within one year) and we deposit in trust a combination of cash and U.S. government or U.S. government agency obligations that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

Under current U.S. federal income tax law, the deposit and our legal release from the senior debt securities would be treated as a taxable event, and beneficial owners of such debt securities would generally recognize any gain or loss on such senior debt securities. Purchasers of the senior debt securities should consult their own advisers with respect to the tax consequences to them of such deposit and discharge, including the applicability and effect of tax laws other than the U.S. federal income tax law.

Defeasance. Unless the applicable prospectus supplement provides otherwise, the following discussion of legal defeasance and discharge and covenant defeasance will apply to any series of senior debt securities issued under the indentures.

Legal Defeasance. We can legally release ourselves from any payment or other obligations on the senior debt securities of any series (called "legal defeasance") if certain conditions are met, including the following:

- We deposit in trust for your benefit and the benefit of all other direct holders of the senior debt securities of the same series a combination of cash and U.S. government or U.S. government agency obligations that will generate enough cash to make interest, principal and any other payments on the senior debt securities of that series on their various due dates.

- We deliver to the trustee an opinion of counsel reasonably acceptable to the trustee confirming that as a result of a change in law, the beneficial owners of the outstanding debt securities of such series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of such legal defeasance and will be subject to U.S. federal income tax on the same amounts, in the same manner and at the same times as would have been the case if such legal defeasance had not occurred.

If we ever did accomplish legal defeasance, as described above, you would have to rely solely on the trust deposit for repayment of the debt securities. You could not look to us for repayment in the event of any shortfall.

Covenant Defeasance. Without any change of current U.S. federal tax law, we can make the same type of deposit described above and be released from some of the covenants in the debt securities (called "covenant defeasance"). In that event, you would lose the protection of those covenants but would gain the protection of having money and securities set aside in trust to repay the debt securities. In order to achieve covenant defeasance, we must do the following (among other things):

- We must deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series a combination of cash and U.S. government or U.S. government agency obligations that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

- We must deliver to the trustee an opinion of counsel reasonably acceptable to the trustee confirming that the beneficial owners of the outstanding debt securities of such series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of such covenant defeasance and will be subject to U.S. federal income tax on the same amounts, in the same manner and at the same times as would have been the case if such covenant defeasance had not occurred.

If we accomplish covenant defeasance, you can still look to us for repayment of the debt securities if there were a shortfall in the trust deposit. In fact, if one of the events of default occurred (such as our bankruptcy) and the debt securities become immediately due and payable, there may be such a shortfall. Depending on the events causing the default, you may not be able to obtain payment of the shortfall.

Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities without the consent of any holder:

- to convey, transfer, assign, mortgage or pledge any assets as security for the senior debt securities of one or more series;

- to evidence the succession of a corporation, limited liability company, partnership or trust to us, and the assumption by such successor of our covenants, agreements and obligations under the senior indenture;

- to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default;

- to cure any ambiguity, defect or inconsistency in the senior indenture or in any supplemental indenture or to conform the senior indenture or the senior debt securities to the description of senior debt securities of such series set forth in this prospectus or any applicable prospectus supplement;

- to provide for or add guarantors with respect to the senior debt securities of any series;

- to establish the form or forms or terms of the senior debt securities as permitted by the senior indenture;
- to evidence and provide for the acceptance of appointment under the senior indenture by a successor trustee, or to make such changes as shall be necessary to provide for or facilitate the administration of the trusts in the senior indenture by more than one trustee;
- to add to, delete from or revise the conditions, limitations and restrictions on the authorized amount, terms, purposes of issue, authentication and delivery of any series of senior debt securities;
- to make any change to the senior debt securities of any series so long as no senior debt securities of such series are outstanding;
- to create additional series of senior debt securities under the senior indenture; or
- to make any change that does not adversely affect the rights of any holder in any material respect.

Other amendments and modifications of the senior indenture or the senior debt securities issued may be made, and our compliance with any provision of the senior indenture with respect to any series of senior debt securities may be waived, with the consent of the holders of a majority of the aggregate principal amount of the outstanding senior debt securities of each series affected by the amendment or modification (each such series voting as a separate class); provided, however, that each affected holder must consent to any modification, amendment or waiver that:

- extends the final maturity of any senior debt securities of such series;
- reduces the principal amount of on any senior debt securities of such series;
- reduces the rate or extends the time of payment of interest on any senior debt securities of such series;
- reduces the amount payable upon the redemption of any senior debt securities of such series;
- changes the currency of payment of principal of or interest on any senior debt securities of such series;
- reduces the principal amount of original issue discount securities payable upon acceleration of maturity or the amount provable in bankruptcy;
- waives a default in the payment of principal of or interest on the senior debt securities;
- changes the provisions relating to the waiver of past defaults or changes or impairs the right of holders to receive payment or to institute suit for the enforcement of any payment or conversion of any senior debt securities of such series on or after the due date therefor;
- modifies any of the provisions of these restrictions on amendments and modifications, except to increase any required percentage or to provide that certain other provisions cannot be modified or waived without the consent of the holder of each senior debt security of such series affected by the modification; or
- reduces the above-stated percentage of outstanding senior debt securities of such series whose holders must consent to a supplemental indenture or to modify or amend or to waive certain provisions of or defaults under the senior indenture.

It shall not be necessary for the holders to approve the particular form of any proposed amendment, supplement or waiver, but it shall be sufficient if the holders' consent approves the substance thereof. After an amendment, supplement or waiver of the senior indenture in accordance

with the provisions described in this section becomes effective, the trustee must give to the holders affected thereby certain notice briefly describing the amendment, supplement or waiver. Any failure by the trustee to give such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such amendment, supplemental indenture or waiver.

No Personal Liability of Incorporators, Stockholders, Officers, Directors. The senior indenture provides that no recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the senior debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the senior debt securities, waives and releases all such liability.

Concerning the Trustee. The senior indenture provides that, except during the continuance of an event of default, the trustee will not be liable except for the performance of such duties as are specifically set forth in the senior indenture. If an event of default has occurred and is continuing, the trustee will exercise such rights and powers vested in it under the senior indenture and will use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

The senior indenture and the provisions of the Trust Indenture Act of 1939 incorporated by reference therein contain limitations on the rights of the trustee thereunder, should it become a creditor of ours or any of our subsidiaries, to obtain payment of claims in certain cases or to realize on certain property received by it in respect of any such claims, as security or otherwise. The trustee is permitted to engage in other transactions, provided that if it acquires any conflicting interest (as defined in the Trust Indenture Act), it must eliminate such conflict or resign.

We may have normal banking relationships with the senior trustee in the ordinary course of business.

Unclaimed Funds. All funds deposited with the trustee or any paying agent for the payment of principal, premium, interest or additional amounts in respect of the senior debt securities that remain unclaimed for two years after the date upon which such principal, premium or interest became due and payable will be repaid to us. Thereafter, any right of any holder of senior debt securities to such funds shall be enforceable only against us, and the trustee and paying agents will have no liability therefor.

Governing Law. The senior indenture and the senior debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

Certain Terms of the Subordinated Debt Securities

Other than the terms of the subordinated indenture and subordinated debt securities relating to subordination or otherwise as described in the prospectus supplement relating to a particular series of subordinated debt securities, the terms of the subordinated indenture and subordinated debt securities are identical in all material respects to the terms of the senior indenture and senior debt securities.

Additional or different subordination terms may be specified in the prospectus supplement applicable to a particular series.

Subordination. The indebtedness evidenced by the subordinated debt securities is subordinate to the prior payment in full of all of our senior indebtedness, as defined in the subordinated indenture. During the continuance beyond any applicable grace period of any default in the payment of principal, premium, interest or any other payment due on any of our senior indebtedness, we may not make any payment of principal of or interest on the subordinated debt securities (except for certain sinking fund

payments). In addition, upon any payment or distribution of our assets upon any dissolution, winding-up, liquidation or reorganization, the payment of the principal of and interest on the subordinated debt securities will be subordinated to the extent provided in the subordinated indenture in right of payment to the prior payment in full of all our senior indebtedness. Because of this subordination, if we dissolve or otherwise liquidate, holders of our subordinated debt securities may receive less, ratably, than holders of our senior indebtedness. The subordination provisions do not prevent the occurrence of an event of default under the subordinated indenture.

The term "senior indebtedness" of a person means with respect to such person the principal of, premium, if any, interest on, and any other payment due pursuant to any of the following, whether outstanding on the date of the subordinated indenture or incurred by that person in the future:

- all of the indebtedness of that person for money borrowed;
- all of the indebtedness of that person evidenced by notes, debentures, bonds or other securities sold by that person for money;
- all of the lease obligations which are capitalized on the books of that person in accordance with generally accepted accounting principles;
- all indebtedness of others of the kinds described in the first two bullet points above and all lease obligations of others of the kind described in the third bullet point above that the person, in any manner, assumes or guarantees or that the person in effect guarantees through an agreement to purchase, whether that agreement is contingent or otherwise; and
- all renewals, extensions or refundings of indebtedness of the kinds described in the first, second or fourth bullet point above and all renewals or extensions of leases of the kinds described in the third or fourth bullet point above; unless, in the case of any particular indebtedness, renewal, extension or refunding, the instrument creating or evidencing it or the assumption or guarantee relating to it expressly provides that such indebtedness, renewal, extension or refunding is not superior in right of payment to the subordinated debt securities. Our senior debt securities constitute senior indebtedness for purposes of the subordinated debt indenture.

DESCRIPTION OF CAPITAL STOCK

General

The following description of our capital stock is intended as a summary only. This description is based upon, and is qualified in its entirety by reference to, our Third Amended and Restated Certificate of Incorporation and Second Amended and Restated By-Laws, each as amended (copies of which are incorporated by reference herein as exhibits to the registration statement of which this prospectus forms a part) and applicable provisions of Delaware corporate law. References in this prospectus to our certificate of incorporation or by-laws mean our certificate of incorporation and by-laws, each as amended.

Our authorized capital stock consists of 187,500,000 shares of common stock, par value $0.001 per share, and 5,000,000 shares of undesignated preferred stock, par value $1.00 per share. As of June 20, 2019, there were 74,052,728 shares of common stock outstanding (excluding 3,013,143 shares held in treasury) and no shares of preferred stock were outstanding.

Common Stock

Voting Rights

Each holder of our common stock is entitled to one vote for each share held on all matters to be voted upon by stockholders. Holders of our common stock do not have cumulative voting rights.

Dividends

The holders of our common stock, after any preferences of holders of any preferred stock, are entitled to receive proportionally any dividends when and if declared by the board of directors out of legally available funds.

Liquidation, Dissolution or Winding-Up

Upon our liquidation, dissolution or winding-up, the holders of our common stock will be entitled to share equally in all assets available for distribution to stockholders, subject to preferences that may apply to shares of preferred stock outstanding at that time. The amount available for common stockholders is calculated after payment of liabilities.

Other Rights

Holders of our common stock have no preemptive, subscription, redemption or conversion rights. Holders of our common stock are not required to make additional capital contributions.

Preferred Stock

As of the date of this prospectus, no shares of preferred stock were outstanding. The terms of any series of preferred stock will be described in the prospectus supplement relating to that series of preferred stock. The terms of any series of preferred stock may differ from the terms described below. Certain provisions of the preferred stock described below and in any applicable prospectus supplement are not complete.

We are authorized to issue "blank check" preferred stock, which may be issued in one or more series upon authorization of our board of directors. Our board of directors is authorized to fix the designation of the series, the number of authorized shares of the series, dividend rights and terms, conversion rights, voting rights, redemption rights and terms, liquidation preferences and any other rights, powers, preferences and limitations applicable to each series of preferred stock. The authorized shares of our preferred stock are available for issuance without further action by our stockholders,

unless such action is required by applicable law or the rules of any stock exchange on which our securities may be listed. If the approval of our stockholders is not required for the issuance of shares of our preferred stock, our board may determine not to seek stockholder approval.

A series of our preferred stock could, depending on the terms of such series, impede the completion of a merger, tender offer or other takeover attempt. Our board of directors will make any determination to issue such shares based upon its judgment as to the best interests of our stockholders. Our directors, in so acting, could issue preferred stock having terms that could discourage an acquisition attempt through which an acquirer may be able to change the composition of our board of directors, including a tender offer or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which stockholders might receive a premium for their stock over the then-current market price of the stock.

The preferred stock has the terms described below unless otherwise provided in the prospectus supplement relating to a particular series of preferred stock. You should read the prospectus supplement relating to the particular series of preferred stock being offered for specific terms, including:

- the designation and stated value per share of the preferred stock and the number of shares offered;
- the amount of liquidation preference per share;
- the price at which the preferred stock will be issued;
- the dividend rate, or method of calculation of dividends, the dates on which dividends will be payable, whether dividends will be cumulative or noncumulative and, if cumulative, the dates from which dividends will commence to accumulate;
- any redemption or sinking fund provisions;
- if other than the currency of the United States, the currency or currencies including composite currencies in which the preferred stock is denominated and/or in which payments will or may be payable;
- any conversion provisions;
- whether we have elected to offer depositary shares as described below under "Description of Depositary Shares;" and
- any other rights, preferences, privileges, limitations and restrictions on the preferred stock.

The preferred stock will, when issued, be fully paid and nonassessable. Unless otherwise specified in the prospectus supplement, each series of preferred stock will rank equally as to dividends and liquidation rights in all respects with each other series of preferred stock. The rights of holders of shares of each series of preferred stock will be subordinate to those of our general creditors.

As described under "Description of Depositary Shares," we may, at our option, with respect to any series of preferred stock, elect to offer fractional interests in shares of preferred stock, and provide for the issuance of depositary receipts representing depositary shares, each of which will represent a fractional interest in a share of the series of preferred stock. The fractional interest will be specified in the prospectus supplement relating to a particular series of preferred stock.

Rank. Unless otherwise specified in the prospectus supplement, the preferred stock will, with respect to dividend rights and rights upon our liquidation, dissolution or winding up of its affairs, rank:

- senior to our common stock and to all equity securities ranking junior to such preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs;
- on a parity with all equity securities issued by us, the terms of which specifically provide that such equity securities rank on a parity with the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs; and
- junior to all equity securities issued by us, the terms of which specifically provide that such equity securities rank senior to the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs.

The term "equity securities" does not include convertible debt securities.

Dividends. Holders of the preferred stock of each series will be entitled to receive, when, as and if declared by our board of directors, cash dividends at such rates and on such dates described in the prospectus supplement. Different series of preferred stock may be entitled to dividends at different rates or based on different methods of calculation. The dividend rate may be fixed or variable or both. Dividends will be payable to the holders of record as they appear on our stock books on record dates fixed by our board of directors, as specified in the applicable prospectus supplement.

Dividends on any series of preferred stock may be cumulative or noncumulative, as described in the applicable prospectus supplement. If our board of directors does not declare a dividend payable on a dividend payment date on any series of noncumulative preferred stock, then the holders of that noncumulative preferred stock will have no right to receive a dividend for that dividend payment date, and we will have no obligation to pay the dividend accrued for that period, whether or not dividends on that series are declared payable on any future dividend payment dates. Dividends on any series of cumulative preferred stock will accrue from the date we initially issue shares of such series or such other date specified in the applicable prospectus supplement.

No dividends may be declared or paid or funds set apart for the payment of any dividends on any parity securities unless full dividends have been paid or set apart for payment on the preferred stock. If full dividends are not paid, the preferred stock will share dividends pro rata with the parity securities.

No dividends may be declared or paid or funds set apart for the payment of dividends on any junior securities unless full dividends for all dividend periods terminating on or prior to the date of the declaration or payment will have been paid or declared and a sum sufficient for the payment set apart for payment on the preferred stock.

Liquidation Preference. Upon any voluntary or involuntary liquidation, dissolution or winding up of our affairs, before we make any distribution or payment to the holders of any common stock or any other class or series of our capital stock ranking junior to the preferred stock in the distribution of assets upon any liquidation, dissolution or winding up of our affairs, the holders of each series of preferred stock shall be entitled to receive out of assets legally available for distribution to stockholders, liquidating distributions in the amount of the liquidation preference per share set forth in the prospectus supplement, plus any accrued and unpaid dividends thereon. Such dividends will not include any accumulation in respect of unpaid noncumulative dividends for prior dividend periods. Unless otherwise specified in the prospectus supplement, after payment of the full amount of their liquidating distributions, the holders of preferred stock will have no right or claim to any of our remaining assets. Upon any such voluntary or involuntary liquidation, dissolution or winding up, if our available assets are insufficient to pay the amount of the liquidating distributions on all outstanding preferred stock and the corresponding amounts payable on all other classes or series of our capital

stock ranking on parity with the preferred stock and all other such classes or series of shares of capital stock ranking on parity with the preferred stock in the distribution of assets, then the holders of the preferred stock and all other such classes or series of capital stock will share ratably in any such distribution of assets in proportion to the full liquidating distributions to which they would otherwise be entitled.

Upon any such liquidation, dissolution or winding up and if we have made liquidating distributions in full to all holders of preferred stock, we will distribute our remaining assets among the holders of any other classes or series of capital stock ranking junior to the preferred stock according to their respective rights and preferences and, in each case, according to their respective number of shares. For such purposes, our consolidation or merger with or into any other corporation, trust or entity, or the sale, lease or conveyance of all or substantially all of our property or assets will not be deemed to constitute a liquidation, dissolution or winding up of our affairs.

Redemption. If so provided in the applicable prospectus supplement, the preferred stock will be subject to mandatory redemption or redemption at our option, as a whole or in part, in each case upon the terms, at the times and at the redemption prices set forth in such prospectus supplement.

The prospectus supplement relating to a series of preferred stock that is subject to mandatory redemption will specify the number of shares of preferred stock that shall be redeemed by us in each year commencing after a date to be specified, at a redemption price per share to be specified, together with an amount equal to all accrued and unpaid dividends thereon to the date of redemption. Unless the shares have a cumulative dividend, such accrued dividends will not include any accumulation in respect of unpaid dividends for prior dividend periods. We may pay the redemption price in cash or other property, as specified in the applicable prospectus supplement. If the redemption price for preferred stock of any series is payable only from the net proceeds of the issuance of shares of our capital stock, the terms of such preferred stock may provide that, if no such shares of our capital stock shall have been issued or to the extent the net proceeds from any issuance are insufficient to pay in full the aggregate redemption price then due, such preferred stock shall automatically and mandatorily be converted into the applicable shares of our capital stock pursuant to conversion provisions specified in the applicable prospectus supplement. Notwithstanding the foregoing, we will not redeem any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on the preferred stock for all past dividend periods and the then current dividend period; or

- if such series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends for the then current dividend period.

In addition, we will not acquire any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on all outstanding shares of such series of preferred stock for all past dividend periods and the then current dividend period; or

- if that series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends on the preferred stock of such series for the then current dividend period.

However, at any time we may purchase or acquire preferred stock of that series (1) pursuant to a purchase or exchange offer made on the same terms to holders of all outstanding preferred stock of

such series or (2) by conversion into or exchange for shares of our capital stock ranking junior to the preferred stock of such series as to dividends and upon liquidation.

If fewer than all of the outstanding shares of preferred stock of any series are to be redeemed, we will determine the number of shares that may be redeemed pro rata from the holders of record of such shares in proportion to the number of such shares held or for which redemption is requested by such holder or by any other equitable manner that we determine. Such determination will reflect adjustments to avoid redemption of fractional shares.

Unless otherwise specified in the prospectus supplement, we will mail notice of redemption at least 30 days but not more than 60 days before the redemption date to each holder of record of preferred stock to be redeemed at the address shown on our stock transfer books. Each notice shall state:

- the redemption date;
- the number of shares and series of preferred stock to be redeemed;
- the redemption price;
- the place or places where certificates for such preferred stock are to be surrendered for payment of the redemption price;
- that dividends on the shares to be redeemed will cease to accrue on such redemption date;
- the date on which the holder's conversion rights, if any, as to such shares shall terminate; and
- the specific number of shares to be redeemed from each such holder if fewer than all the shares of any series are to be redeemed.

If notice of redemption has been given and we have set aside the funds necessary for such redemption in trust for the benefit of the holders of any shares called for redemption, then from and after the redemption date, dividends will cease to accrue on such shares, and all rights of the holders of such shares will terminate, except the right to receive the redemption price.

Voting Rights. Holders of preferred stock will not have any voting rights, except as required by law or as indicated in the applicable prospectus supplement.

Unless otherwise provided for under the terms of any series of preferred stock, no consent or vote of the holders of shares of preferred stock or any series thereof shall be required for any amendment to our certificate of incorporation that would increase the number of authorized shares of preferred stock or the number of authorized shares of any series thereof or decrease the number of authorized shares of preferred stock or the number of authorized shares of any series thereof (but not below the number of authorized shares of preferred stock or such series, as the case may be, then outstanding).

Conversion Rights. The terms and conditions, if any, upon which any series of preferred stock is convertible into our common stock will be set forth in the applicable prospectus supplement relating thereto. Such terms will include the number of shares of common stock into which the shares of preferred stock are convertible, the conversion price, rate or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at our option or at the option of the holders of the preferred stock, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption.

Transfer Agent and Registrar. The transfer agent and registrar for the preferred stock will be set forth in the applicable prospectus supplement.

Effects of Authorized but Unissued Stock

We have shares of common stock and preferred stock available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of The NASDAQ Global Select Market. We may utilize these additional shares for a variety of corporate purposes, including for future public offerings to raise additional capital, or facilitate corporate acquisitions or for payment as a dividend on our capital stock. The existence of unissued and unreserved common stock and preferred stock may enable our board of directors to issue shares to persons friendly to current management or to issue preferred stock with terms that could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a controlling interest in our company by means of a merger, tender offer, proxy contest or otherwise. In addition, if we issue preferred stock, the issuance could adversely affect the voting power of holders of common stock, and the likelihood that such holders will receive dividend payments and payments upon liquidation.

Provisions of our Certificate of Incorporation and By-Laws and Delaware Law That May Have Anti-Takeover Effects

Removal of directors by stockholders

Our directors may be removed with or without cause by the affirmative vote of the holders of at least 75% of the votes which all stockholders would be entitled to cast in any annual election of directors.

Stockholder nomination of directors

Our by-laws provide that a stockholder must notify us in writing of any stockholder nomination of a director in the case of an election of directors at an annual meeting of stockholders, not less than 90 days nor more than 120 days prior to the first anniversary of the preceding year's annual meeting; provided, however, that in the event that the date of the annual meeting in any other year is advanced by more than 30 days, or delayed by more than 60 days, from the first anniversary of the preceding year's annual meeting, a stockholder's notice must be so received no earlier than the one hundred twentieth day prior to such annual meeting and not later than the close of business on the later of the ninetieth day prior to such annual meeting and the tenth day following the day on which notice of the date of such annual meeting was disclosed in a press release reported by a national news service or in a document we file with the SEC. In the case of an election of directors at a special meeting of stockholders, a stockholder must notify us in writing of any stockholder nomination of a director not earlier than the one hundred twentieth day prior to such special meeting and not later than the close of business on the later of the ninetieth day prior to such special meeting and the tenth day following the day on which notice of the date of such special meeting was disclosed in a press release reported by a national news service or in a document we file with the SEC.

No action by written consent

Our certificate of incorporation provides that our stockholders may not act by written consent and may only act at duly called meetings of stockholders.

Delaware business combination statute

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that such person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and

stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which such person became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Super-majority voting

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless a corporation's certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our by-laws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors or class of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors or class of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

Limitation of Liability and Indemnification Matters

Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director's duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- for voting or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the Delaware General Corporation Law is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the Delaware General Corporation Law.

Our certificate of incorporation provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors

or executive officers, we have been informed that in the opinion of the SEC such indemnification is against public policy and is therefore unenforceable.

Transfer Agent and Registrar

American Stock Transfer & Trust Company is transfer agent and registrar for our common stock.

NASDAQ Global Select Market

Our common stock is listed on The NASDAQ Global Select Market under the symbol "MDCO".

DESCRIPTION OF DEPOSITARY SHARES

General

We may, at our option, elect to offer fractional shares of preferred stock, which we call depositary shares, rather than full shares of preferred stock. If we do, we will issue to the public receipts, called depositary receipts, for depositary shares, each of which will represent a fraction, to be described in the applicable prospectus supplement, of a share of a particular series of preferred stock. Unless otherwise provided in the prospectus supplement, each owner of a depositary share will be entitled, in proportion to the applicable fractional interest in a share of preferred stock represented by the depositary share, to all the rights and preferences of the preferred stock represented by the depositary share. Those rights include dividend, voting, redemption, conversion and liquidation rights.

The shares of preferred stock underlying the depositary shares will be deposited with a bank or trust company selected by us to act as depositary under a deposit agreement between us, the depositary and the holders of the depositary receipts. The depositary will be the transfer agent, registrar and dividend disbursing agent for the depositary shares.

The depositary shares will be evidenced by depositary receipts issued pursuant to the deposit agreement. Holders of depositary receipts agree to be bound by the deposit agreement, which requires holders to take certain actions such as filing proof of residence and paying certain charges.

The summary of terms of the depositary shares contained in this prospectus is not complete. You should refer to the form of the deposit agreement, our certificate of incorporation and the certificate of designation for the applicable series of preferred stock that are, or will be, filed with the SEC.

Dividends and Other Distributions

The depositary will distribute all cash dividends or other cash distributions, if any, received in respect of the preferred stock underlying the depositary shares to the record holders of depositary shares in proportion to the numbers of depositary shares owned by those holders on the relevant record date. The relevant record date for depositary shares will be the same date as the record date for the underlying preferred stock.

If there is a distribution other than in cash, the depositary will distribute property (including securities) received by it to the record holders of depositary shares, unless the depositary determines that it is not feasible to make the distribution. If this occurs, the depositary may, with our approval, adopt another method for the distribution, including selling the property and distributing the net proceeds from the sale to the holders.

Liquidation Preference

If a series of preferred stock underlying the depositary shares has a liquidation preference, in the event of the voluntary or involuntary liquidation, dissolution or winding up of us, holders of depositary shares will be entitled to receive the fraction of the liquidation preference accorded each share of the applicable series of preferred stock, as set forth in the applicable prospectus supplement.

Withdrawal of Stock

Unless the related depositary shares have been previously called for redemption, upon surrender of the depositary receipts at the office of the depositary, the holder of the depositary shares will be entitled to delivery, at the office of the depositary to or upon his or her order, of the number of whole shares of the preferred stock and any money or other property represented by the depositary shares. If the depositary receipts delivered by the holder evidence a number of depositary shares in excess of the number of depositary shares representing the number of whole shares of preferred stock to be

withdrawn, the depositary will deliver to the holder at the same time a new depositary receipt evidencing the excess number of depositary shares. In no event will the depositary deliver fractional shares of preferred stock upon surrender of depositary receipts. Holders of preferred stock thus withdrawn may not thereafter deposit those shares under the deposit agreement or receive depositary receipts evidencing depositary shares therefor.

Redemption of Depositary Shares

Whenever we redeem shares of preferred stock held by the depositary, the depositary will redeem as of the same redemption date the number of depositary shares representing shares of the preferred stock so redeemed, so long as we have paid in full to the depositary the redemption price of the preferred stock to be redeemed plus an amount equal to any accumulated and unpaid dividends on the preferred stock to the date fixed for redemption. The redemption price per depositary share will be equal to the redemption price and any other amounts per share payable on the preferred stock multiplied by the fraction of a share of preferred stock represented by one depositary share. If less than all the depositary shares are to be redeemed, the depositary shares to be redeemed will be selected by lot or pro rata or by any other equitable method as may be determined by the depositary.

After the date fixed for redemption, depositary shares called for redemption will no longer be deemed to be outstanding and all rights of the holders of depositary shares will cease, except the right to receive the monies payable upon redemption and any money or other property to which the holders of the depositary shares were entitled upon redemption upon surrender to the depositary of the depositary receipts evidencing the depositary shares.

Voting the Preferred Stock

Upon receipt of notice of any meeting at which the holders of the preferred stock are entitled to vote, the depositary will mail the information contained in the notice of meeting to the record holders of the depositary receipts relating to that preferred stock. The record date for the depositary receipts relating to the preferred stock will be the same date as the record date for the preferred stock. Each record holder of the depositary shares on the record date will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the number of shares of preferred stock represented by that holder's depositary shares. The depositary will endeavor, insofar as practicable, to vote the number of shares of preferred stock represented by the depositary shares in accordance with those instructions, and we will agree to take all action that may be deemed necessary by the depositary in order to enable the depositary to do so. The depositary will not vote any shares of preferred stock except to the extent it receives specific instructions from the holders of depositary shares representing that number of shares of preferred stock.

Charges of Depositary

We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangements. We will pay charges of the depositary in connection with the initial deposit of the preferred stock and any redemption of the preferred stock. Holders of depositary receipts will pay transfer, income and other taxes and governmental charges and such other charges (including those in connection with the receipt and distribution of dividends, the sale or exercise of rights, the withdrawal of the preferred stock and the transferring, splitting or grouping of depositary receipts) as are expressly provided in the deposit agreement to be for their accounts. If these charges have not been paid by the holders of depositary receipts, the depositary may refuse to transfer depositary shares, withhold dividends and distributions and sell the depositary shares evidenced by the depositary receipt.

Amendment and Termination of the Deposit Agreement

The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may be amended by agreement between us and the depositary. However, any amendment that materially and adversely alters the rights of the holders of depositary shares, other than fee changes, will not be effective unless the amendment has been approved by the holders of a majority of the outstanding depositary shares. The deposit agreement may be terminated by the depositary or us only if:

- all outstanding depositary shares have been redeemed; or
- there has been a final distribution of the preferred stock in connection with our dissolution and such distribution has been made to all the holders of depositary shares.

Resignation and Removal of Depositary

The depositary may resign at any time by delivering to us notice of its election to do so, and we may remove the depositary at any time. Any resignation or removal of the depositary will take effect upon our appointment of a successor depositary and its acceptance of such appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having the requisite combined capital and surplus as set forth in the applicable agreement.

Notices

The depositary will forward to holders of depositary receipts all notices, reports and other communications, including proxy solicitation materials received from us, that are delivered to the depositary and that we are required to furnish to the holders of the preferred stock. In addition, the depositary will make available for inspection by holders of depositary receipts at the principal office of the depositary, and at such other places as it may from time to time deem advisable, any reports and communications we deliver to the depositary as the holder of preferred stock.

Limitation of Liability

Neither we nor the depositary will be liable if either is prevented or delayed by law or any circumstance beyond its control in performing its obligations. Our obligations and those of the depositary will be limited to performance in good faith of our and their duties thereunder. We and the depositary will not be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or preferred stock unless satisfactory indemnity is furnished. We and the depositary may rely upon written advice of counsel or accountants, on information provided by persons presenting preferred stock for deposit, holders of depositary receipts or other persons believed to be competent to give such information and on documents believed to be genuine and to have been signed or presented by the proper party or parties.

DESCRIPTION OF PURCHASE CONTRACTS AND PURCHASE UNITS

We may issue purchase contracts, including contracts obligating holders to purchase from or sell to us, and obligating us to sell to or purchase from the holders, a specified number of shares of our common stock, preferred stock or depositary shares at a future date or dates, which we refer to in this prospectus as purchase contracts. The price per share of common stock, preferred stock or depositary shares and the number of shares of each may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula set forth in the purchase contracts. The purchase contracts may be issued separately or as part of units, often known as purchase units, consisting of one or more purchase contracts and beneficial interests in debt securities or any other securities described in the applicable prospectus supplement or any combination of the foregoing, securing the holders' obligations to purchase the common stock, preferred stock or depositary shares under the purchase contracts.

The purchase contracts may require us to make periodic payments to the holders of the purchase units or vice versa, and these payments may be unsecured or prefunded on some basis. The purchase contracts may require holders to secure their obligations under those contracts in a specified manner, including pledging their interest in another purchase contract.

The applicable prospectus supplement will describe the terms of the purchase contracts and purchase units, including, if applicable, collateral or depositary arrangements.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase debt securities, common stock, preferred stock or depositary shares. We may offer warrants separately or together with one or more additional warrants, debt securities, common stock, preferred stock or depositary shares, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following:

- the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants are to be sold separately or with other securities as parts of units;
- whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of any equity securities purchasable upon exercise of the warrants;
- the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the debt securities, common stock, preferred stock or depositary shares with which the warrants are issued and, the number of warrants issued with each security;
- if applicable, the date from and after which any warrants issued as part of a unit and the related debt securities, common stock, preferred stock or depositary shares will be separately transferable;
- the number of shares of common stock, the number of shares of preferred stock or the number of depositary shares purchasable upon exercise of a warrant and the price at which those shares may be purchased;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the antidilution provisions of, and other provisions for changes to or adjustment in the exercise price of, the warrants, if any;
- any redemption or call provisions; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

FORMS OF SECURITIES

Each debt security, depositary share, purchase contract, purchase unit and warrant will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Unless the applicable prospectus supplement provides otherwise, certificated securities in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depositary or its nominee as the owner of the debt securities, depositary shares, purchase contracts, purchase units or warrants represented by these global securities. The depositary maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Registered Global Securities

We may issue the registered debt securities, depositary shares, purchase contracts, purchase units and warrants in the form of one or more fully registered global securities that will be deposited with a depositary or its nominee identified in the applicable prospectus supplement and registered in the name of that depositary or nominee. In those cases, one or more registered global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by registered global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a registered global security may not be transferred except as a whole by and among the depositary for the registered global security, the nominees of the depositary or any successors of the depositary or those nominees.

If not described below, any specific terms of the depositary arrangement with respect to any securities to be represented by a registered global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depositary arrangements.

Ownership of beneficial interests in a registered global security will be limited to persons, called participants, that have accounts with the depositary or persons that may hold interests through participants. Upon the issuance of a registered global security, the depositary will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a registered global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depositary, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in registered global securities.

So long as the depositary, or its nominee, is the registered owner of a registered global security, that depositary or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the registered global security for all purposes under the applicable indenture, deposit agreement, purchase contract, warrant agreement or purchase unit agreement. Except as described below, owners of beneficial interests in a registered global security will not be entitled to have the securities represented by the registered global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the applicable indenture, deposit agreement,

purchase contract, purchase unit agreement or warrant agreement. Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depositary for that registered global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable indenture, deposit agreement, purchase contract, purchase unit agreement or warrant agreement. We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a registered global security desires to give or take any action that a holder is entitled to give or take under the applicable indenture, deposit agreement, purchase contract, purchase unit agreement or warrant agreement, the depositary for the registered global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal, premium, if any, and interest payments on debt securities, and any payments to holders with respect to depositary shares, warrants, purchase agreements or purchase units, represented by a registered global security registered in the name of a depositary or its nominee will be made to the depositary or its nominee, as the case may be, as the registered owner of the registered global security. None of us, the trustees, the warrant agents, the unit agents or any other agent of ours, agent of the trustees or agent of the warrant agents or unit agents will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the registered global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depositary for any of the securities represented by a registered global security, upon receipt of any payment to holders of principal, premium, interest or other distribution of underlying securities or other property on that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that registered global security as shown on the records of the depositary. We also expect that payments by participants to owners of beneficial interests in a registered global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers or registered in "street name," and will be the responsibility of those participants.

If the depositary for any of the securities represented by a registered global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Exchange Act, and a successor depositary registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the registered global security that had been held by the depositary. Any securities issued in definitive form in exchange for a registered global security will be registered in the name or names that the depositary gives to the relevant trustee, warrant agent, unit agent or other relevant agent of ours or theirs. It is expected that the depositary's instructions will be based upon directions received by the depositary from participants with respect to ownership of beneficial interests in the registered global security that had been held by the depositary.

PLAN OF DISTRIBUTION

We may sell securities:

- to or through underwriters;
- through dealers;
- through agents;
- directly to purchasers; or
- through a combination of any of these methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act, and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

If a dealer is utilized in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are

expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus is being delivered will be passed upon by Paul, Weiss, Rifkind, Wharton & Garrison LLP.

EXPERTS

The consolidated financial statements of The Medicines Company appearing in The Medicines Company's Annual Report (Form 10-K) for the year ended December 31, 2018, and the effectiveness of The Medicines Company's internal control over financial reporting as of December 31, 2018, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon included therein, and incorporated herein by reference. Such financial statements and The Medicines Company management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2018 are, and audited financial statements and The Medicines Company management's assessment of the effectiveness of internal control over financial reporting to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements and the effectiveness of our internal control over financial reporting as of the respective dates (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

$150,000,000

THE MEDICINES COMPANY

Common Stock

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Goldman Sachs & Co. LLC **J.P. Morgan**

June , 2019