Alkermes plc.
Form 10-K
February 15, 2019
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10 K

(Mark One)

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

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission file number: 001 35299

ALKERMES PUBLIC LIMITED COMPANY

(Exact name of registrant as specified in its charter)

Ireland	98 1007018
(State or other jurisdiction of	(I.R.S. Employer
incorporation or organization)	Identification No.)
Connaught House	(Zip code)
1 Burlington Road	

Dublin 4, Ireland
(Address of principal executive offices)

+353 1 772 8000

(Registrant's telephone number, including area code)

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

Title of each class	Name of each exchange on which registered
Ordinary shares, $0.01 par value	Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: None

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

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

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

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

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

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

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

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

Exchange Act.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b 2 of the Act). Yes No

The aggregate market value of the registrant's ordinary shares held by non affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the ordinary shares were last sold as of the last business day of the registrant's most recently completed second fiscal quarter was $6,322,607,110.

As of February 4, 2019, 156,039,212 ordinary shares were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement for our 2019 Annual General Meeting of Shareholders are incorporated by reference into Part III of this report.

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ALKERMES PLC AND

SUBSIDIARIES

ANNUAL REPORT ON FORM 10 K

FOR THE YEAR ENDED DECEMBER 31, 2018

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CAUTIONARY NOTE CONCERNING FORWARD LOOKING STATEMENTS

This document contains and incorporates by reference "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"). In some cases, these statements can be identified by the use of forward looking terminology such as "may," "will," "could," "should," "would," "expect," "anticipate," "continue," "believe," "plan," "estimate other similar words. These statements discuss future expectations and contain projections of results of operations or of financial condition, or state trends and known uncertainties or other forward looking information. Forward looking statements in this Annual Report on Form 10 K ("Annual Report") include, without limitation, statements regarding:

- our expectations regarding our financial performance, including revenues, expenses, gross margins, liquidity, capital expenditures and income taxes;
- our expectations regarding our products, including those expectations related to product development, regulatory filings, regulatory approvals and regulatory timelines, therapeutic and commercial scope and potential, and the costs and expenses related to such activities;
- our expectations regarding the initiation, timing and results of clinical trials of our products;
- our expectations regarding the competitive landscape, and changes therein, related to our products, including competition from generic forms of our products or competitive products and competitive development programs;
- our expectations regarding the financial impact of currency exchange rate fluctuations and valuations;
- our expectations regarding future amortization of intangible assets;
- our expectations regarding our collaborations, licensing arrangements and other significant agreements with third parties relating to our products, including our development programs;
- our expectations regarding the impact of new legislation and related regulations and the adoption of new accounting pronouncements;
- our expectations regarding near term changes in the nature of our market risk exposures or in management's objectives and strategies with respect to managing such exposures;
- our ability to comply with restrictive covenants of our indebtedness and our ability to fund our debt service obligations;
- our expectations regarding future capital requirements and capital expenditures and our ability to finance our operations and capital requirements;
- our expectations regarding the timing, outcome and impact of administrative, regulatory, legal and other proceedings related to our patents, other proprietary and intellectual property ("IP") rights, and our products; and
- other factors discussed elsewhere in this Annual Report.

Actual results might differ materially from those expressed or implied by these forward looking statements because these forward looking statements are subject to risks, assumptions and uncertainties. You are cautioned not to place undue reliance on forward looking statements, which speak only as of the date of this Annual Report. All subsequent written and oral forward looking statements concerning the matters addressed in this Annual Report and attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. Except as required by applicable law or regulation, we do not undertake any obligation to update publicly or revise any forward looking statements, whether as a result of new information, future events or otherwise. In light of these risks, assumptions and uncertainties, the forward looking events discussed in this Annual Report might not occur. For more information regarding the risks and uncertainties of our business, see "Item 1A—Risk Factors" in this Annual Report.

This Annual Report includes data that we obtained from industry publications and third-party research, surveys and studies. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. This Annual Report also includes data based on our own internal estimates and research. Our internal estimates and research have not been verified by any independent source, and, while we believe the industry

publications and third-party research, surveys and studies are reliable, we have not independently verified such data. Such third-party data and our internal estimates and research are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in “Item 1A—Risk Factors” in this Annual Report. These and other factors could cause results to differ materially from those expressed in this Annual Report.

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NOTE REGARDING COMPANY AND PRODUCT REFERENCES

Use of the terms such as “us,” “we,” “our,” “Alkermes” or the “Company” in this Annual Report is meant to refer to Alkermes plc and its consolidated subsidiaries. Except as otherwise suggested by the context, (a) references to “products” or “our products” in this Annual Report include our marketed products, marketed products using our proprietary technologies, our product candidates, product candidates using our proprietary technologies, development products and development products using our proprietary technologies, (b) references to the “biopharmaceutical industry” in this Annual Report are intended to include reference to the “biotechnology industry” and/or the “pharmaceutical industry” and (c) references to “licensees” are used interchangeably with references to “partners.”

NOTE REGARDING TRADEMARKS

We are the owner of various United States (“U.S.”) federal trademark registrations (“®”) and other trademarks (“™”), including ALKERMES®, ARISTADA®, ARISTADA INITIO®, CODAS®, IPDAS®, LinkeRx®, MXDAS®, NanoCrystal®, SODAS®, and VIVITROL®.

The following are trademarks of the respective companies listed: ABILIFY® and ABILIFY MAINTENA®—Otsuka Pharmaceutical Co., Ltd. (“Otsuka Pharm. Co.”); AMPYRA® and FAMPYRA®—Acorda Therapeutics, Inc. (“Acorda”); ANTABUSE®—Teva Women’s Health, Inc.; AUBAGIO® and LEMTRADA®—Sanofi Societe Anonyme France; AVONEX®, PLEGRIDY®, TECFIDERA®, and TYSABRI®—Biogen MA Inc. (together with its affiliates, “Biogen”); BETASERON®—Bayer Pharma AG; BRIXADI®—Braeburn Inc.; BUNAVAIL™—BioDelivery Sciences; BYDUREON®—Amylin Pharmaceuticals, LLC (“Amylin”); BYDUREON BCise™—AstraZeneca Pharmaceuticals LP;—CAMPRAL®—Merck Sante; COPAXONE®—Teva Pharmaceutical Industries Ltd.; EXTAVIA® and GILENYA®—Novartis AG; INVEGA SUSTENNA®, RISPERDAL CONSTA® INVEGA TRINZA®, TREVICTA® and XEPLION®—Johnson & Johnson (or its affiliates); LATUDA®—Dainippon Sumitomo Pharma Co., Ltd.; NOVANTRONE® and REBIF®—Ares Trading S.A.; OCREVUS®—Genentech, Inc. (“Genentech”); PROBUPHINE®—Titan Pharmaceuticals, Inc.; REXULTI®— H. Lundbeck A/S plc; PERSERIS®— SUBOXONE®, SUBUTEX® and SUBLOCADE®—Indivior plc (or its affiliates); VICTOZA®—Novo Nordisk A/S LLC; ZUBSOLV®—Orexo US, Inc.; ZYPREXA® RELPREVV®—Eli Lilly and Company; and VRAYLAR®— Forest Laboratories, LLC . Other trademarks, trade names and service marks appearing in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Annual Report are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

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PART I

Item 1.Business

The following discussion contains forward looking statements. Actual results may differ significantly from those expressed or implied in the forward looking statements. See "Cautionary Note Concerning Forward Looking Statements" on page 3 of this Annual Report. Factors that might cause future results to differ materially from those expressed or implied in the forward looking statements include, but are not limited to, those discussed in "Item 1A—Risk Factors" and elsewhere in this Annual Report.

Overview

Alkermes plc is a fully integrated, global biopharmaceutical company that applies its scientific expertise and proprietary technologies to research, develop and commercialize, both with partners and on its own, pharmaceutical products that are designed to address unmet medical needs of patients in major therapeutic areas. Alkermes has a diversified portfolio of marketed drug products and a clinical pipeline of product candidates focused on central nervous system ("CNS") disorders such as schizophrenia, depression, addiction and multiple sclerosis ("MS"), and oncology. Headquartered in Dublin, Ireland, Alkermes has a research and development ("R&D") center in Waltham, Massachusetts; an R&D and manufacturing facility in Athlone, Ireland; and a manufacturing facility in Wilmington, Ohio.

Marketed Products

The key marketed products discussed below are expected to generate significant revenues for us. Refer to the "Patents and Proprietary Rights" section of this Annual Report for information with respect to the intellectual property protection for these marketed products.

Summary information regarding our proprietary products:

Product	Indication(s)	Licensee	Territory
	Initiation or re-initiation of ARISTADA for the treatment of Schizophrenia	None	Commercialized by Alkermes in the U.S.
	Schizophrenia	None	Commercialized by Alkermes in the U.S.
	Alcohol	None	Commercialized by

dependence and		Alkermes in the U.S.
Opioid dependence		
	Cilag GmbH International (“Cilag”)	Russia and Commonwealth of Independent States (“CIS”)

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Summary information regarding products that use our proprietary technologies:

Product	Indication(s)	Licensee	Territory
RISPERDAL CONSTA	Schizophrenia and Bipolar I disorder	Janssen Pharmaceutica Inc. (“Janssen, Inc.”) and Janssen Pharmaceutica International, a division of Cilag International AG (“Janssen International”)	Worldwide
INVEGA SUSTENNA	Schizophrenia and Schizoaffective disorder	Janssen Pharmaceutica N.V. (together with Janssen, Inc., Janssen International and their affiliates “Janssen”)	U.S.
XEPLION	Schizophrenia	Janssen	All countries outside of the U.S. (“ROW”)

INVEGA TRINZA	Schizophrenia	Janssen	U.S.
TREVICTA	Schizophrenia	Janssen	ROW
AMPYRA FAMPYRA	Treatment to improve walking in patients with MS, as demonstrated by an increase in walking speed	Acorda Biogen, under sublicense from Acorda	U.S. ROW

Proprietary Products

We develop and commercialize products designed to address the unmet needs of patients suffering from addiction and schizophrenia.

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ARISTADA

ARISTADA (aripiprazole lauroxil) is an extended-release intramuscular injectable suspension approved in the U.S. for the treatment of schizophrenia. ARISTADA is the first of our products to utilize our proprietary LinkeRx technology. ARISTADA is a prodrug; once in the body, ARISTADA is likely converted by enzyme-mediated hydrolysis to N-hydroxymethyl aripiprazole, which is then hydrolyzed to aripiprazole. ARISTADA is the first atypical antipsychotic with four dosing options—once-monthly (441 mg, 662 mg, 882 mg), once-every-six-weeks (882 mg) and once-every-two-months (1064 mg)— to deliver and maintain therapeutic levels of medication in the body. ARISTADA is packaged in a ready-to-use, pre-filled product format. We developed ARISTADA and manufacture and commercialize it in the U.S.

ARISTADA INITIO

ARISTADA INITIO (aripiprazole lauroxil), in combination with a single 30 mg dose of oral aripiprazole, is indicated for the initiation of ARISTADA when used for the treatment of schizophrenia in adults. ARISTADA INITIO leverages our proprietary NanoCrystal technology and provides an extended-release formulation of aripiprazole lauroxil in a smaller particle size compared to ARISTADA. This smaller particle size enables faster dissolution and leads to more rapid achievement of relevant levels of aripiprazole. The ARISTADA INITIO regimen, consisting of a single injection of 675 mg ARISTADA INITIO in combination with a single 30 mg dose of oral aripiprazole, when used to initiate onto any dose of ARISTADA, provides patients with relevant levels of aripiprazole within four days of treatment initiation. The first ARISTADA dose may be administered on the same day as the ARISTADA INITIO regimen or up to 10 days thereafter. We developed ARISTADA INITIO and exclusively manufacture and commercialize it in the U.S.

What is schizophrenia?

Schizophrenia is a chronic, severe and disabling brain disorder. The disease is marked by positive symptoms (hallucinations and delusions) and negative symptoms (depression, blunted emotions and social withdrawal), as well as by disorganized thinking. Approximately 3.5 million people are diagnosed with schizophrenia in the U.S., with men and women affected equally. Worldwide, it is estimated that one person in every 100 develops schizophrenia. Studies have demonstrated that as many as 75% of patients with schizophrenia have difficulty taking their oral medication on a regular basis, which can lead to worsening of symptoms.

VIVITROL

VIVITROL (naltrexone for extended-release injectable suspension) is a once-monthly, non-narcotic, injectable medication approved in the U.S., Russia and certain countries of the CIS for the treatment of alcohol dependence and for the prevention of relapse to opioid dependence, following opioid detoxification. VIVITROL uses our polymer-based microsphere injectable extended-release technology to deliver and maintain therapeutic medication levels in the body through one intramuscular injection every four weeks. We developed and exclusively manufacture VIVITROL. We commercialize VIVITROL in the U.S., and Cilag commercializes VIVITROL in Russia and certain countries of the CIS.

For a discussion of legal proceedings related to the patents covering VIVITROL, see Note 16, Commitments and Contingent Liabilities in the “Notes to Consolidated Financial Statements” and “Item 3—Legal Proceedings” in this Annual Report, and for information about risks relating to such legal proceedings, see “Part I, Item 1A—Risk Factors” in this Annual Report and specifically the sections entitled “— Patent protection for our products is important and uncertain,” “— Uncertainty over intellectual property in the biopharmaceutical industry has been the source of litigation, which is inherently costly and unpredictable, could significantly delay or prevent approval or commercialization of our

products, and could adversely affect our business" and ""— Litigation, arbitration or regulatory action (such as citizens petitions) filed against regulatory agencies related to our product or Alkermes, including securities litigation, may result in financial losses, harm our reputation, divert management resources, negatively impact the approval of our products, or otherwise negatively impact our business."

What are opioid dependence and alcohol dependence?

Opioid dependence is a serious and chronic brain disease characterized by compulsive, prolonged self-administration of opioid substances that are not used for a medical purpose. According to the 2017 U.S. National Survey on Drug Use and Health, an estimated 2.0 million people aged 18 or older in the U.S. had an opioid use disorder. In 2013, with the publication of the Diagnostic Statistical Manual (DSM) V, the DSM IV diagnoses of substance use disorders as either dependence or abuse (i.e., opioid dependence), were combined into one diagnostic category of "substance use disorders" (i.e., opioid use disorder) with three categories of disorder severity—either mild, moderate or severe. It is believed that the DSM IV diagnoses of opioid dependence corresponds to the DSM V diagnosis of either moderate or severe opioid use disorder.

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Alcohol dependence is a serious and chronic brain disease characterized by cravings for alcohol, loss of control over drinking, withdrawal symptoms and an increased tolerance for alcohol. According to the 2017 U.S. National Survey on Drug Use and Health, an estimated 7.8 million people had alcohol dependence. Adherence to medication is particularly challenging with this patient population.

Products Using Our Proprietary Technologies

We have granted licenses under our proprietary technologies to enable third parties to develop, commercialize and, in some cases, manufacture products for which we receive royalties and/or manufacturing revenues. Such arrangements include the following:

INVEGA SUSTENNA/XEPLION, INVEGA TRINZA/TREVICTA and RISPERDAL CONSTA

INVEGA SUSTENNA/XEPLION (paliperidone palmitate), INVEGA TRINZA/TREVICTA (paliperidone palmitate 3-month injection) and RISPERDAL CONSTA (risperidone long-acting injection) are long-acting atypical antipsychotics owned and commercialized worldwide by Janssen that incorporate our proprietary technologies.

INVEGA SUSTENNA is approved in the U.S. for the treatment of schizophrenia and for the treatment of schizoaffective disorder as either a monotherapy or adjunctive therapy. Paliperidone palmitate extended-release injectable suspension is approved in the European Union ("EU") and other countries outside of the U.S. for the treatment of schizophrenia and is marketed and sold under the trade name XEPLION. INVEGA SUSTENNA/XEPLION uses our nanoparticle injectable extended-release technology to increase the rate of dissolution and enable the formulation of an aqueous suspension for once-monthly intramuscular administration. INVEGA SUSTENNA/XEPLION is manufactured by Janssen. For a discussion of legal proceedings related to the patents covering INVEGA SUSTENNA, see Note 16, Commitments and Contingent Liabilities in the "Notes to Consolidated Financial Statements" and "Item 3—Legal Proceedings" in this Annual Report and for information about risks relating to such legal proceedings, see "Part I, Item 1A—Risk Factors" in this Annual Report and specifically the section entitled "—We or our licensees may face claims against intellectual property rights covering our products and competition from generic drug manufacturers."

INVEGA TRINZA/TREVICTA is an atypical antipsychotic injection for the treatment of schizophrenia used in people who have been treated with INVEGA SUSTENNA for at least four months. INVEGA TRINZA/TREVICTA is the first schizophrenia treatment to be taken once every three months. TREVICTA is approved in the EU for the maintenance treatment of schizophrenia in adult patients who are clinically stable on XEPLION. INVEGA TRINZA/TREVICTA uses our proprietary technology and is manufactured by Janssen.

RISPERDAL CONSTA is approved in the U.S. for the treatment of schizophrenia and as both monotherapy and adjunctive therapy to lithium or valproate in the maintenance treatment of bipolar I disorder. RISPERDAL CONSTA is approved in numerous countries outside of the U.S. for the treatment of schizophrenia and the maintenance treatment of bipolar I disorder. RISPERDAL CONSTA uses our polymer-based microsphere injectable extended-release technology to deliver and maintain therapeutic medication levels in the body through just one intramuscular injection every two weeks. RISPERDAL CONSTA microspheres are exclusively manufactured by us. For a discussion of legal proceedings related to one of the patents covering RISPERDAL CONSTA, see Note 16, Commitments and Contingent Liabilities in the "Notes to Consolidated Financial Statements" and "Item 3—Legal Proceedings" in this Annual Report and for information about risks relating to such legal proceedings, see "Part I, Item 1A—Risk Factors" in this Annual Report and specifically the section entitled "—We or our licensees may face claims against intellectual property rights covering our products and competition from generic drug manufacturers."

Revenues from Janssen accounted for approximately 29%, 33% and 36% of our consolidated revenues for the years ended December 31, 2018, 2017 and 2016, respectively. See “Collaborative Arrangements” in Part I of this Annual Report for information about our relationship with Janssen.

What is bipolar I disorder?

Bipolar I disorder is a brain disorder that causes unusual shifts in a person’s mood, energy and ability to function. It is often characterized by debilitating mood swings, from extreme highs (mania) to extreme lows (depression). Bipolar I disorder is characterized based on the occurrence of at least one manic episode, with or without the occurrence of a major depressive episode and affects approximately one percent of the American adult population in any given year. The median age of onset for bipolar I disorder is 25 years.

What is schizoaffective disorder?

Schizoaffective disorder is a condition in which a person experiences a combination of schizophrenia symptoms, such as delusions, hallucinations or other symptoms characteristic of schizophrenia, and mood disorder symptoms, such as mania or depression. Schizoaffective disorder is a serious mental illness that affects about one in 100 people.

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AMPYRA/FAMPYRA

AMPYRA (dalfampridine)/FAMPYRA (fampridine) is believed to be the first treatment approved in the U.S. and in over 50 countries across Europe, Asia and the Americas to improve walking in adults with MS who have walking disability, as demonstrated by an increase in walking speed. Extended-release dalfampridine tablets are marketed and sold by Acorda in the U.S. under the trade name AMPYRA and by Biogen outside the U.S. under the trade name FAMPYRA. FAMPYRA is approved in the EU for the improvement of walking in adults with MS. AMPYRA and FAMPYRA incorporate our oral controlled-release technology. AMPYRA (including the authorized generic version of AMPYRA) and FAMPYRA are manufactured by us.

For a discussion of legal proceedings related to the patents covering AMPYRA, see Note 16, Commitments and Contingent Liabilities in the "Notes to Consolidated Financial Statements" and "Item 3—Legal Proceedings" in this Annual Report and for information about risks relating to such legal proceedings, see "Part I, Item 1A—Risk Factors" in this Annual Report and specifically the section entitled "—We or our licensees may face claims against intellectual property rights covering our products and competition from generic drug manufacturers." The legal proceedings related to the patents covering AMPYRA do not involve the patents covering FAMPYRA, and the latest of the patents covering FAMPYRA expires in April 2025 in the EU.

Starting in September 2018, generic versions of AMPYRA, including the authorized generic version of AMPYRA, began to enter the U.S. market.

What is multiple sclerosis?

Multiple sclerosis, or MS, is a chronic, usually progressive, disease in which the immune system attacks and degrades the function of nerve fibers in the brain and spinal cord. These nerve fibers consist of long, thin fibers, or axons, surrounded by a myelin sheath, which facilitates the transmission of electrical impulses. In MS, the myelin sheath is damaged by the body's own immune system, causing areas of myelin sheath loss, also known as demyelination. This damage, which can occur at multiple sites in the CNS, blocks or diminishes conduction of electrical impulses. People with MS may suffer impairments in any number of neurological functions. These impairments vary from individual to individual and over the course of time, depending on which parts of the brain and spinal cord are affected, and often include difficulty walking. Individuals vary in the severity of the impairments they suffer on a day to day basis, with impairments becoming better or worse depending on the activity of the disease on a given day.

Key Development Programs

Our R&D is focused on leveraging our formulation expertise and proprietary product platforms to develop novel, competitively advantaged medications designed to enhance patient outcomes in major CNS disorders, such as schizophrenia, addiction, depression and MS, and in oncology. As part of our ongoing R&D efforts, we have devoted, and will continue to devote, significant resources to conducting pre-clinical work and clinical studies to advance the development of new pharmaceutical products. The discussion below highlights our current key R&D programs. Drug development involves a high degree of risk and investment, and the status, timing and scope of our development programs are subject to change. Important factors that could adversely affect our drug development efforts are discussed in "Part I, Item 1A—Risk Factors" of this Annual Report. Refer to the "Patents and Proprietary Rights" section in "Part I, Item 1— Business" of this Annual Report for information with respect to the intellectual property protection for our development candidates.

Diroximel Fumarate (BIIB098)

Diroximel fumarate (“BIIB098”), formerly referred to as ALKS 8700, is a novel, oral fumarate in development for the treatment of relapsing forms of MS. Diroximel fumarate is designed to rapidly convert to monomethyl fumarate in the body and may have the potential to offer differentiated gastrointestinal tolerability due to its chemical structure as compared to the currently marketed dimethyl fumarate, TECFIDERA.

The pivotal clinical program for diroximel fumarate consists of pharmacokinetic bridging studies comparing diroximel fumarate and TECFIDERA and a two-year, multicenter, open-label study designed to assess the safety of BIIB098, which we initiated in December 2015. We submitted a 505(b)(2) NDA for diroximel fumarate in December 2018. For more information about 505(b)(2) NDAs, see “Part 1, Item 1—Business, Regulatory, Hatch-Waxman Act” of this Annual Report. In addition, EVOLVE-MS-2, an elective, randomized, head-to-head phase 3 study of the gastrointestinal tolerability of diroximel fumarate versus TECFIDERA is ongoing, with topline results expected in mid-2019.

In November 2017, we entered into an exclusive license and collaboration agreement with Biogen relating to diroximel fumarate. Revenues from Biogen related to this license and collaboration agreement accounted for approximately 10% and less than 10% of our consolidated revenues for the years ended December 31, 2018 and 2017, respectively. For more information about the license and collaboration agreement with Biogen, see “Part 1, Item 1—Business, Collaborative Arrangements” of this Annual Report.

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ALKS 3831

ALKS 3831 is an investigational, novel, once-daily, oral atypical antipsychotic drug candidate for the treatment of schizophrenia. ALKS 3831 is composed of samidorphan, a novel, new molecular entity, co-formulated with the established antipsychotic agent, olanzapine, in a single bilayer tablet. ALKS 3831 is designed to provide the strong antipsychotic efficacy of olanzapine with a favorable weight profile.

The ENLIGHTEN clinical development program for ALKS 3831 includes two key studies: ENLIGHTEN-1, a four-week study evaluating the antipsychotic efficacy of ALKS 3831 compared to placebo, and ENLIGHTEN-2, a six-month study assessing weight gain with ALKS 3831 compared to olanzapine in patients with schizophrenia. The program also includes supportive studies to evaluate the pharmacokinetic and metabolic profile and long-term safety of ALKS 3831.

In June 2017, we announced positive topline results from ENLIGHTEN-1, a multinational, double-blind, randomized, phase 3 study that evaluated the antipsychotic efficacy, safety and tolerability of ALKS 3831 compared to placebo over a four-week period in patients experiencing an acute exacerbation of schizophrenia. ALKS 3831 met the prespecified primary endpoint demonstrating statistically significant reductions from baseline in Positive and Negative Syndrome Scale (“PANSS”) scores compared to placebo. The study also included an olanzapine arm but was not designed to provide comparative efficacy or safety data between ALKS 3831 and olanzapine. Data from the study showed that olanzapine achieved similar improvements from baseline PANSS scores as compared to placebo.

In November 2018, we announced positive topline results from ENLIGHTEN-2, a multicenter, double-blind, randomized, phase 3 study that evaluated the weight gain profile of ALKS 3831 compared to olanzapine in patients with stable schizophrenia over a six-month period. ALKS 3831 met the prespecified co-primary endpoints, demonstrating both a lower mean percent weight gain from baseline at six months compared to the olanzapine group, and a lower proportion of patients who gained 10% or more of their baseline body weight at six months compared to the olanzapine group. We plan to present ENLIGHTEN-2 data at a medical meeting in the first half of 2019.

We will request a pre-NDA meeting with the FDA to discuss its key requirements including the efficacy, safety, weight and metabolic profile of ALKS 3831, and plan to submit an NDA for ALKS 3831 in mid-2019.

ALKS 4230

ALKS 4230 is a novel, engineered fusion protein designed to selectively activate tumor-killing immune cells while avoiding the expansion of immunosuppressive cells by preferentially binding to the intermediate affinity interleukin-2 (“IL-2”) receptor complex. The selectivity of ALKS 4230 is designed to leverage the proven anti-tumor effects of existing IL-2 therapy, while mitigating certain limitations. Our phase 1 study for ALKS 4230 is designed to evaluate ALKS 4230 as a monotherapy agent and in combination with the anti-PD-1 therapy, pembrolizumab.

A dose-escalation stage designed to determine a maximum tolerated dose of ALKS 4230 in a monotherapy setting and to identify the optimal dose range of ALKS 4230 based on measures of immunological-pharmacodynamic effects is ongoing. Upon completion of the dose-escalation stage, we expect to initiate a monotherapy dose-expansion stage of the phase 1 study in patients with renal cell carcinoma or melanoma. Initial data from the dose-escalation stage of the phase 1 study, demonstrating dose-dependent pharmacodynamic effects on circulating CD8+ T cells and natural killer cells with minimal and non-dose dependent effect on immunosuppressive regulatory T cells, were presented at the 2018 Society for Immunotherapy of Cancer meeting.

In September 2018, we initiated the combination therapy stage of the phase 1 study, designed to assess the safety profile and anti-tumor activity of ALKS 4230 with pembrolizumab in patients with select advanced solid tumors.

ALKS 5461 Update

ALKS 5461 is a proprietary, once-daily, oral investigational medicine with a novel mechanism of action for the adjunctive treatment of major depressive disorder (“MDD”) in patients with an inadequate response to standard antidepressant therapies. ALKS 5461 is a fixed-dose combination of buprenorphine, a partial mu-opioid receptor agonist and kappa-opioid receptor antagonist, and samidorphan, a mu-opioid receptor antagonist.

The clinical development program for ALKS 5461 included three core phase 3 efficacy studies (FORWARD-3, FORWARD-4 and FORWARD-5), as well as additional supportive studies to evaluate the long-term safety, dosing, pharmacokinetic profile and human abuse potential of ALKS 5461. Our NDA for ALKS 5461, submitted to the FDA in January 2018, and accepted for review by the FDA in April 2018 after the issuance, and then rescission, of a refusal to file letter, was based on a comprehensive clinical efficacy and safety package with data from more than 30 clinical trials and more than 1,500 patients with MDD.

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As previously disclosed, on November 1, 2018, the FDA convened an advisory committee meeting for the ALKS 5461 NDA. The Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee jointly voted that the benefit-risk profile was not adequate to support approval of ALKS 5461. On February 1, 2019, we announced receipt of a complete response letter, or CRL, from the FDA for the ALKS 5461 NDA. The CRL states that the FDA is unable to approve the ALKS 5461 NDA in its present form and requests additional clinical data to provide substantial evidence of effectiveness of ALKS 5461 for the adjunctive treatment of MDD. We plan to meet with the FDA to discuss the contents of the CRL and potential next steps for ALKS 5461. This interaction with the Agency will inform whether there is a viable path forward for the ALKS 5461 program.

Collaborative Arrangements

We have entered into several collaborative arrangements to develop and commercialize products and, in connection with such arrangements, to access technological, financial, marketing, manufacturing and other resources. Refer to the "Patents and Proprietary Rights" section in this "Part I, Item 1—Business" of this Annual Report for information with respect to the intellectual property protection for these products.

Janssen

INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA

Under our license agreement with Janssen Pharmaceutica N.V., we granted Janssen a worldwide exclusive license under our NanoCrystal technology to develop, commercialize and manufacture INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA and related products.

Under this license agreement, we received milestone payments upon the achievement of certain development goals from Janssen; there are no further milestones to be earned under this agreement. We receive tiered royalty payments between 5% and 9% of INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA end-market net sales in each country where the license is in effect, with the exact royalty percentage determined based on aggregate worldwide net sales. The tiered royalty payments consist of a patent royalty and a know how royalty, both of which are determined on a country by country basis. The patent royalty, which equals 1.5% of net sales, is payable in each country until the expiration of the last of the patents claiming the product in such country. The know how royalty is a tiered royalty of 3.5%, 5.5% and 7.5% on aggregate worldwide net sales of below $250 million, between $250 million and $500 million, and greater than $500 million, respectively. The know how royalty is payable for the later of 15 years from first commercial sale of a product in each individual country or March 31, 2019, subject in each case to the expiry of the license agreement. These royalty payments may be reduced in any country based on patent litigation or on competing products achieving certain minimum sales thresholds. The license agreement expires upon the later of (i) March 31, 2019 or (ii) the expiration of the last of the patents subject to the agreement. After expiration, Janssen retains a non exclusive, royalty free license to develop, manufacture and commercialize the products.

Janssen may terminate the license agreement in whole or in part upon three months' notice to us. We and Janssen have the right to terminate the agreement upon a material breach of the other party, which is not cured within a certain time period, or upon the other party's bankruptcy or insolvency.

RISPERDAL CONSTA

Under a product development agreement, we collaborated with Janssen on the development of RISPERDAL CONSTA. Under the development agreement, Janssen provided funding to us for the development of RISPERDAL CONSTA, and Janssen is responsible for securing all necessary regulatory approvals for the product.

Under two license agreements, we granted Janssen and an affiliate of Janssen exclusive worldwide licenses to use and sell RISPERDAL CONSTA. Under our license agreements with Janssen, we receive royalty payments equal to 2.5% of Janssen's end-market net sales of RISPERDAL CONSTA in each country where the license is in effect based on the quarter when the product is sold by Janssen. This royalty may be reduced in any country based on lack of patent coverage and significant competition from generic versions of the product. Janssen can terminate the license agreements upon 30 days' prior written notice to us. Either party may terminate the license agreements by written notice following a breach which continues for 90 days after the delivery of written notice thereof or upon the other party's insolvency. The licenses granted to Janssen expire on a country by country basis upon the later of (i) the expiration of the last patent claiming the product in such country or (ii) 15 years after the date of the first commercial sale of the product in such country, provided that in no event will the license granted to Janssen expire later than the twentieth anniversary of the first commercial sale of the product in each such country, with the exception of Canada, France, Germany, Italy, Japan, Spain and the United Kingdom, in each case, where the fifteen year minimum shall pertain regardless. After expiration, Janssen retains a non exclusive, royalty free license to manufacture, use and sell RISPERDAL CONSTA.

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We exclusively manufacture RISPERDAL CONSTA for commercial sale. Under our manufacturing and supply agreement with Janssen, we record manufacturing revenues when product is shipped to Janssen, based on a percentage of Janssen's net unit sales price for RISPERDAL CONSTA for the applicable calendar year. This percentage is determined based on Janssen's unit demand for such calendar year and varies based on the volume of units shipped, with a minimum manufacturing fee of 7.5%. Either party may terminate the manufacturing and supply agreement upon a material breach by the other party, which is not resolved within 60 days after receipt of a written notice specifying the material breach or upon written notice in the event of the other party's insolvency or bankruptcy. Janssen may terminate the agreement upon six months' written notice to us. In the event that Janssen terminates the manufacturing and supply agreement without terminating the license agreements, the royalty rate payable to us on Janssen's net sales of RISPERDAL CONSTA would increase from 2.5% to 5.0%.

Acorda

Under an amended and restated license agreement, we granted Acorda an exclusive worldwide license to use and sell and, solely in accordance with our supply agreement, to make or have made, AMPYRA/FAMPYRA. We receive certain commercial and development milestone payments, license revenues and a royalty of approximately 10% based on net sales of AMPYRA (including the authorized generic version of AMPYRA) and FAMPYRA by Acorda and its sub licensee, Biogen. This royalty payment may be reduced in any country based on lack of patent coverage, competing products achieving certain minimum sales thresholds, and whether we manufacture the product.

In June 2009, we entered into an amendment of the amended and restated license agreement and the supply agreement with Acorda and, pursuant to such amendment, consented to the sublicense by Acorda to Biogen of Acorda's rights to use and sell FAMPYRA in certain territories outside of the U.S. (to the extent that such rights were to be sublicensed to Biogen pursuant to its separate collaboration and license agreement with Acorda). Under this amendment, we agreed to modify certain terms and conditions of the amended and restated license agreement and the supply agreement with Acorda to reflect the sublicense by Acorda to Biogen.

Acorda has the right to terminate the amended and restated license agreement upon 90 days' written notice. We have the right to terminate the amended and restated license agreement for countries in which Acorda fails to launch a product within a specified time after obtaining the necessary regulatory approval or fails to file regulatory approvals within a commercially reasonable time after completion of, and receipt of positive data from, all pre-clinical and clinical studies required for filing a marketing authorization application. Either party has the right to terminate the amended and restated license agreement by written notice following a material breach of the other party, which is not cured within a certain time period, or upon the other party's entry into bankruptcy or dissolution proceedings. If we terminate Acorda's license in any country, we are entitled to a license from Acorda of its patent rights and know how relating to the product as well as the related data, information and regulatory files, and to market the product in the applicable country, subject to an initial payment equal to Acorda's cost of developing such data, information and regulatory files and to ongoing royalty payments to Acorda. Subject to the termination of the amended and restated license agreement, licenses granted under the license agreement terminate on a country by country basis upon the expiration of the last to expire of our patents or the existence of a threshold level of competition in the marketplace.

Under our commercial manufacturing supply agreement with Acorda, we manufacture and supply AMPYRA/FAMPYRA for Acorda (and its sub licensee, Biogen). Under the terms of the agreement, Acorda may obtain up to 25% of its total annual requirements of product from a second source manufacturer. We receive manufacturing royalties equal to 8% of net selling price for all product manufactured by us and a compensating payment for product manufactured and supplied by a third party. We may terminate the commercial manufacturing supply agreement upon 12 months' prior written notice to Acorda, and either party may terminate the commercial manufacturing supply agreement following a material and uncured breach of the commercial manufacturing supply agreement or amended and restated license agreement or the entry into bankruptcy or dissolution proceedings by the

other party. In addition, subject to early termination of the commercial manufacturing supply agreement noted above, the commercial manufacturing supply agreement terminates upon the expiry or termination of the amended and restated license agreement.

We are entitled to receive the following milestone payments under our amended and restated license agreement with Acorda for each of the third and fourth new indications of the product developed thereunder:

- initiation of a phase 3 clinical trial: $1.0 million;
- acceptance of an NDA by the FDA: $1.0 million;
- approval of the NDA by the FDA: $1.5 million; and
- the first commercial sale: $1.5 million.

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Biogen

In November 2017, we entered into a license and collaboration agreement with Biogen, under which we granted Biogen a worldwide, exclusive, sublicensable license to develop, manufacture and commercialize BIIB098 and other products covered by patents licensed to Biogen under the agreement. We amended the license and collaboration agreement in October 2018.

Upon entering into this agreement in November 2017, we received an up-front cash payment of $28.0 million. In June 2018, we received an additional cash payment of $50.0 million following Biogen's review of preliminary gastrointestinal tolerability data from the ongoing clinical development program for BIIB098. We are also eligible to receive an additional cash payment of $150.0 million upon an approval by the FDA on or before December 31, 2021 of a 505(b)(2) NDA (or, in certain circumstances, a 505(b)(1) NDA) for BIIB098. We are also eligible to receive additional payments upon achievement of developmental milestones with respect to the first two products, other than BIIB098, covered by patents licensed to Biogen under the agreement.

In addition, we will receive a mid-teens percentage royalty on worldwide net sales of BIIB098, subject to, under certain circumstances, minimum annual payments for the first five years following FDA approval of BIIB098. We will also receive royalties on net sales of products, other than BIIB098, covered by patents licensed to Biogen under the agreement, at tiered royalty rates calculated as percentages of net sales ranging from high-single digits to sub-teen double digits. All royalties are payable on a product-by-product and country-by-country basis until the later of (i) the last-to-expire patent right covering the applicable product in the applicable country and (ii) a specified period of time from the first commercial sale of the applicable product in the applicable country. Royalties for all such products and the minimum annual payments for BIIB098 are subject to reductions as set forth in the agreement.

Except in certain limited circumstances, until FDA approval of an NDA for BIIB098, we are responsible for the development of BIIB098 for the treatment of MS. Biogen paid a portion of the BIIB098 development costs we incurred in 2017 and, since January 1, 2018, Biogen is responsible for all BIIB098 development costs we incur, subject to annual budget limitations. After the date of FDA approval of an NDA for BIIB098 for the treatment of MS, Biogen will be responsible for all development and commercialization activities, as well as the costs of all such activities, for BIIB098 and all other products covered by patents licensed to Biogen under the agreement. We have retained the right to manufacture clinical supplies and commercial supplies of BIIB098 and all other products covered by patents licensed to Biogen under the agreement, subject to Biogen's right to manufacture or have manufactured commercial supplies as a back-up manufacturer and subject to good faith agreement by the parties on the terms of such manufacturing arrangements.

If BIIB098 discontinuations due to gastrointestinal adverse events in BIIB098's long-term safety clinical trial exceed a certain pre-defined threshold, or, if in part B of the head-to-head phase 3 gastrointestinal tolerability clinical trial, BIIB098 demonstrates a greater rate of discontinuations as compared to TECFIDERA and TECFIDERA demonstrates statistical superiority to BIIB098 on the primary endpoint, then "GI Inferiority" shall be deemed to exist, and (i) Biogen shall have the right to recapture from us its $50.0 million option payment through certain temporary reductions in royalty rates, (ii) the minimum annual payments Biogen owes to us shall terminate and (iii) there shall be no reversion of BIIB098 to us in the event that Biogen terminates the agreement and does not commercialize BIIB098.

Unless earlier terminated, the agreement will remain in effect until the expiry of all royalty obligations. Biogen has the right to terminate the agreement at will, on a product-by-product basis or in its entirety. Either party has the right to terminate the agreement following any governmental prohibition of the transactions effected by the agreement, or in connection with an insolvency event involving the other party. Upon termination of the agreement by either party, if, prior to such termination (i) GI Inferiority was not deemed to exist or (ii) GI Inferiority was deemed to exist but Biogen commercialized BIIB098, then, at our request, the BIIB098 program will revert to us.

Proprietary Product Platforms

Our proprietary product platforms, which include technologies owned and exclusively licensed to us, address several important development opportunities. We have used these technologies as platforms to establish drug development, clinical development and regulatory expertise.

Injectable Extended Release Microsphere Technology

Our injectable extended release microsphere technology allows us to encapsulate small molecule pharmaceuticals, peptides and proteins in microspheres made of common medical polymers. The technology is designed to enable novel formulations of pharmaceuticals by providing controlled, extended release of drugs over time. Drug release from the microsphere is controlled by diffusion of the drug through the microsphere and by biodegradation of the polymer. These processes can be modulated through a number of formulation and fabrication variables, including drug substance and microsphere particle sizing and choice of polymers and excipients.

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LinkeRx Technology

The long acting LinkeRx technology platform is designed to enable the creation of extended release injectable versions of antipsychotic therapies and may also be useful in other disease areas in which extended duration of action may provide therapeutic benefits. The technology uses proprietary linker tail chemistry to create new molecular entities derived from known agents.

NanoCrystal Technology

Our NanoCrystal technology is applicable to poorly water soluble compounds and involves formulating and stabilizing drugs into particles that are nanometers in size. A drug in NanoCrystal form can be incorporated into a range of common dosage forms and administration routes, including tablets, capsules, inhalation devices and sterile forms for injection, with the potential for enhanced oral bioavailability, increased therapeutic effectiveness, reduced/eliminated fed/fasted variability and sustained duration of intravenous/intramuscular release.

Oral Controlled Release Technology

Our oral controlled release ("OCR") technologies are used to formulate, develop and manufacture oral dosage forms of pharmaceutical products that control the release characteristics of standard dosage forms. Our OCR platform includes technologies for tailored pharmacokinetic profiles including SODAS technology, CODAS technology, IPDAS technology and the MXDAS drug absorption system, each as described below:

- SODAS Technology: SODAS ("Spheroidal Oral Drug Absorption System") technology involves producing uniform spherical beads of 1 mm to 2 mm in diameter containing drug plus excipients and coated with product specific modified release polymers. Varying the nature and combination of polymers within a selectively permeable membrane enables varying degrees of modified release depending upon the required product profile.
- CODAS Technology: CODAS ("Chronotherapeutic Oral Drug Absorption System") technology enables the delayed onset of drug release incorporating the use of specific polymers, resulting in a drug release profile that more accurately complements circadian patterns.
- IPDAS Technology: IPDAS ("Intestinal Protective Drug Absorption System") technology conveys gastrointestinal protection by a wide dispersion of drug in a controlled and gradual manner, through the use of numerous high density controlled release beads compressed into a tablet form. Release characteristics are modified by the application of polymers to the micro matrix and subsequent coatings, which form a rate limiting semi permeable membrane.
- MXDAS Technology: MXDAS ("Matrix Drug Absorption System") technology formulates the drug in a hydrophilic matrix and incorporates one or more hydrophilic matrix forming polymers into a solid oral dosage form, which controls the release of drug through a process of diffusion and erosion in the gastrointestinal tract.

Manufacturing and Product Supply

We own and occupy an R&D and manufacturing facility in Athlone, Ireland and a manufacturing facility in Wilmington, Ohio. We either purchase active drug product from third parties or receive it from our third party licensees to formulate product using our technologies. The manufacture of our products for clinical trials and commercial use is subject to Current Good Manufacturing Practices ("cGMP") regulations and other regulations. Our manufacturing and development capabilities include formulation through process development, scale up and full scale commercial manufacturing and specialized capabilities for the development and manufacturing of controlled substances.

Although some materials and services for our products are currently available from a single source or a limited number of qualified sources, we attempt to acquire an adequate inventory of such materials, establish alternative sources and/or negotiate long term supply arrangements. We believe we do not have any significant issues in finding

suppliers. However, we cannot be certain that we will continue to be able to obtain long term supplies of our manufacturing materials.

Our supply chain is growing with an expanding external network of third party service providers involved in the manufacture of our products who are subject to inspection by the FDA or comparable agencies in other jurisdictions. Any delay, interruption or other issues that arise in the acquisition of active pharmaceutical ingredients ("API"), raw materials, or components, or in the manufacture, fill finish, packaging, or storage of our marketed or development products, including as a result of a failure of our facilities or the facilities or operations of third parties to pass any regulatory agency inspection, could significantly impair our ability to sell our products or advance our development efforts, as the case may be. For information about risks relating to the manufacture of our marketed products and product candidates, see "Item 1A—Risk Factors" and specifically those sections entitled "—We rely on third parties to provide services in connection with the manufacture and distribution of our products" and "—We are subject to risks related to the manufacture of our products."

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Proprietary Products and Products using our Proprietary Technologies

We manufacture ARISTADA and ARISTADA INITIO, and microspheres for RISPERDAL CONSTA and VIVITROL, in our Wilmington, Ohio facility. We are currently operating one RISPERDAL CONSTA line, two VIVITROL lines and two ARISTADA lines at commercial scale. We source our packaging operations for VIVITROL, ARISTADA and ARISTADA INITIO to third party contractors. Janssen is responsible for packaging operations for RISPERDAL CONSTA and, in Russia and certain countries of the CIS, VIVITROL. Our Wilmington, Ohio facility has been inspected by U.S., European (including the Medicines and Healthcare Products Regulatory Agency), Chinese, Japanese, Brazilian, Turkish and Saudi Arabian regulatory authorities for compliance with required cGMP standards for continued commercial manufacturing.

We manufacture AMPYRA (including the authorized generic version of AMPYRA)/FAMPYRA and other products in our Athlone, Ireland facility. This facility has been inspected by U.S., Irish, Brazilian, Turkish, Saudi Arabian, Korean, Belarusian and Chinese regulatory authorities for compliance with required cGMP standards for continued commercial manufacturing. In 2018, the FDA completed a pre-approval inspection and recommended the Athlone, Ireland facility for approval to manufacture commercial supplies of bulk intermediate NanoCrystal dispersion of Meloxicam.

For more information about our manufacturing facilities, see “Item 2—Properties.”

Clinical Products

We have established, and are operating, facilities with the capability to produce clinical supplies of injectable extended release products as well as solid dosage and biologics products at our Wilmington, Ohio facility and NanoCrystal and OCR technology products at our Athlone, Ireland facility. We have also contracted with third party manufacturers to formulate certain products for clinical use. We require that our contract manufacturers adhere to cGMP in the manufacture of products for clinical use.

Research & Development

We devote significant resources to R&D programs. We focus our R&D efforts on developing novel therapeutics in areas of high unmet medical need. Our R&D efforts include, but are not limited to, areas such as pharmaceutical formulation, analytical chemistry, process development, engineering, scale up and drug optimization/delivery. Please see “Management’s Discussion and Analysis of Financial Condition and Results of Operations” for our R&D expenditures for our years ended December 31, 2018, 2017 and 2016.

Permits and Regulatory Approvals

We hold various licenses in respect of our manufacturing activities conducted in Wilmington, Ohio and Athlone, Ireland. The primary licenses held in this regard are FDA Registrations of Drug Establishment; and Drug Enforcement Administration of the U.S. Department of Justice (“DEA”). We also hold a Manufacturers Authorization (No. M1067), an Investigational Medicinal Products Manufacturers Authorization (No. IMP074) and Certificates of Good Manufacturing Practice Compliance of a Manufacturer (Ref. 2014/7828/IMP074 and 2014/7828/M1067) from the Health Products Regulatory Authority in Ireland (“HPRA”) in respect of our Athlone, Ireland facility, and a number of Controlled Substance Licenses granted by the HPRA. Due to certain U.S. state law requirements, we also hold state licenses to cover distribution activities through certain states and not in respect of any manufacturing activities conducted in those states.

We do not generally act as the product authorization holder for products incorporating our drug delivery technologies that have been developed on behalf of a licensee of such technologies. In such cases, our licensee usually holds the relevant authorization from the FDA or other national regulator, and we would support this authorization by furnishing a copy of the Drug Master File, or the chemistry, manufacturing and controls data to the relevant regulator to prove adequate manufacturing data in respect of the product. We would generally update this information annually with the relevant regulator. In other cases where we have developed proprietary products, such as VIVITROL, ARISTADA and ARISTADA INITIO, we hold the appropriate regulatory documentation ourselves.

Marketing, Sales and Distribution

We are responsible for the marketing of VIVITROL, ARISTADA and ARISTADA INITIO in the U.S. We focus our sales and marketing efforts on physicians in private practice and in public treatment systems. We believe that we use customary pharmaceutical company practices to market our products and to educate physicians, including through advertisements, professional symposia, selling initiatives and other methods. Our education initiatives extend to individual physicians, nurses, social workers, counselors and other stakeholders involved in the treatment of opioid dependence, alcohol dependence and schizophrenia. We provide, and contract with third party vendors to provide, customer service and other related programs for our products, such as product specific websites, insurance research services and order, delivery and fulfillment services.

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Our sales force for VIVITROL in the U.S. consists of approximately 100 individuals. VIVITROL is primarily sold to pharmaceutical wholesalers, pharmacies, specialty distributors and treatment providers. Product sales of VIVITROL during the year ended December 31, 2018 to Cardinal Health, AmerisourceBergen Corporation ("AmerisourceBergen") and McKesson Corporation represented approximately 23%, 20% and 19%, respectively, of total VIVITROL gross sales.

Our sales force for ARISTADA in the U.S. consists of approximately 300 individuals. ARISTADA is primarily sold to pharmaceutical wholesalers. Product sales of ARISTADA and ARISTADA INITIO during the year ended December 31, 2018 to Cardinal Health, McKesson Corporation and AmerisourceBergen represented approximately 47%, 23% and 19%, respectively, of total ARISTADA gross sales.

ICS, a division of AmerisourceBergen, provides warehousing, shipping and administrative services for VIVITROL, ARISTADA and ARISTADA INITIO.

Under our license agreements with Janssen, Acorda and other licensees and sublicensees, they are each responsible for the commercialization of any products developed under their respective agreement if and when regulatory approval is obtained.

Competition

We face intense competition in the development, manufacture, marketing and commercialization of our products from many and varied sources, such as research institutions and biopharmaceutical companies, including other companies with similar technologies. Some of these competitors are also our licensees, who control the commercialization of products from which we receive manufacturing and royalty revenues. These competitors are working to develop and market other systems, products and other methods of preventing or reducing disease, and new small molecule and other classes of drugs that can be used with or without a drug delivery system.

The biopharmaceutical industry is characterized by intensive research, development and commercialization efforts and rapid and significant technological change. Many of our competitors are larger and have significantly greater financial and other resources than we do. We expect our competitors to develop new technologies, products and processes that may be more effective than those we develop. The development of technologically improved or different products or technologies may make our products or product platforms obsolete or noncompetitive before we recover expenses incurred in connection with their development or realize any revenues from any marketed product.

There are other companies developing extended release product platforms. In many cases, there are products on the market or in development that may be in direct competition with our products. In addition, we know of new chemical entities that are being developed that, if successful, could compete against our products. These chemical entities are being designed to work differently than our products and may turn out to be safer or to be more effective than our products. Among the many experimental therapies being tested around the world, there may be some that we do not now know of that may compete with our proprietary product platforms or products. Our licensees could choose a competing technology to use with their drugs instead of one of our product platforms and could develop products that compete with our products.

With respect to our products, we believe that our ability to successfully compete will depend on, among other things, the existence of competing or alternative products in the marketplace, including generic competition, and the relative price of those products; the efficacy, safety and reliability of our products compared to competing or alternative products; product acceptance by physicians, other health care providers and patients; our ability to comply with applicable laws, regulations and regulatory requirements with respect to the commercialization of our products, including any changes or increases to regulatory restrictions; protection of our proprietary rights; obtaining

reimbursement for our products in approved indications; our ability to complete clinical development and obtain regulatory approvals for our products, and the timing and scope of regulatory approvals; our ability to provide a reliable supply of commercial quantities of a product to the market; and our ability to recruit, retain and develop skilled employees.

With respect to our proprietary injectable product platform, we are aware that there are other companies developing extended-release delivery systems for pharmaceutical products, including, but not limited to Luye Pharma Group Ltd. ("Luye Pharma"), which is developing risperidone formulated as extended release microspheres for intramuscular injection for the treatment of schizophrenia and/or schizoaffective disorders. In the treatment of schizophrenia, ARISTADA, INVEGA SUSTENNA/XEPLION, INVEGA TRINZA/TREVICTA and RISPERDAL CONSTA compete with each other and a number of other injectable products including ZYPREXA RELPREVV ((olanzapine) For Extended Release Injectable Suspension), which is marketed and sold by Lilly; ABILIFY MAINTENA (aripiprazole for extended release injectable suspension), a once-monthly injectable formulation of ABILIFY (aripiprazole) developed by Otsuka Pharm. Co.; PERSERIS (risperidone for extended release injectable suspension), a once-monthly formulation of risperidone marketed by Indivior plc; oral compounds currently on the market; and generic versions of branded oral and injectable products. In the treatment of bipolar disorder, RISPERDAL CONSTA competes with antipsychotics such as oral aripiprazole, REXULTI, LATUDA, VRAYLAR, ABILIFY MAINTENA, risperidone, quetiapine, olanzapine, ziprasidone and clozapine.

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In the treatment of alcohol dependence, VIVITROL competes with generic acamprosate calcium (also known as CAMPRAL) and generic disulfiram (also known as ANTABUSE) as well as currently marketed drugs, including generic drugs, also formulated from naltrexone. Other pharmaceutical companies are developing products that have shown some promise in treating alcohol dependence that, if approved by the FDA, would compete with VIVITROL.

In the treatment of opioid dependence, VIVITROL competes with SUBOXONE (buprenorphine HCl/naloxone HCl dehydrate sublingual tablets), SUBOXONE (buprenorphine/naloxone) Sublingual Film, SUBUTEX (buprenorphine HCl sublingual tablets) and SUBLOCADE (once-monthly buprenorphine extended-release injection), each of which is marketed and sold by Indivior plc, and BUNAVAIL buccal film (buprenorphine and naloxone) marketed by BioDelivery Sciences, PROBUPHINE (buprenorphine) from Titan Pharmaceuticals, Inc., ZUBSOLV (buprenorphine and naloxone) marketed by Orexo US, Inc., and once launched, will compete with BRIXADI, which will be marketed by Braeburn, Inc. VIVITROL also competes with methadone, oral naltrexone and generic versions of SUBUTEX and SUBOXONE sublingual tablets. Other pharmaceutical companies are developing products that have shown promise in treating opioid dependence that, if approved by the FDA, would compete with VIVITROL.

While AMPYRA/FAMPYRA is approved as a treatment to improve walking in patients with MS, there are a number of FDA approved therapies for MS disease management that seek to reduce the frequency and severity of exacerbations or slow the accumulation of physical disability for people with certain types of MS. These products include AVONEX, TYSABRI, TECFIDERA, and PLEGRIDY from Biogen; OCREVUS from Genentech; BETASERON from Bayer HealthCare Pharmaceuticals; COPAXONE from Teva Pharmaceutical Industries Ltd.; REBIF and NOVANTRONE from EMD Serono, Inc.; GILENYA and EXTAVIA from Novartis AG; AUBAGIO and LEMTRADA from Sanofi Aventis; and generic products, including generic versions of AMPYRA.

With respect to our NanoCrystal technology, we are aware that other technology approaches similarly address poorly water soluble drugs. These approaches include nanoparticles, cyclodextrins, lipid based self emulsifying drug delivery systems, dendrimers and micelles, among others, any of which could limit the potential success and growth prospects of products incorporating our NanoCrystal technology. In addition, there are many competing technologies to our OCR technology, some of which are owned by large pharmaceutical companies with drug delivery divisions and other, smaller drug delivery specific companies.

Patents and Proprietary Rights

Our success will be dependent, in part, on our ability to obtain and maintain patent protection for our products, including those marketed and sold by our licensees, to maintain trade secret protection and to operate without infringing upon the proprietary rights of others. We have a proprietary portfolio of patent rights and exclusive licenses to patents and patent applications, which includes numerous patents in the U.S. and in other countries directed to compositions of matter, methods of treatment and formulations, as well as processes of preparation. In the future, we plan to file additional patent applications in the U.S. and in other countries directed to new or improved products and processes, and we intend to vigorously defend our patent positions. In addition, our licensees may own additional patents that cover those products owned by such licensees that incorporate our proprietary technologies and for which we receive royalties.

ARISTADA and ARISTADA INITIO

We have several U.S. patents and patent applications, and a number of corresponding foreign counterparts, that cover ARISTADA and/or ARISTADA INITIO. Our principal U.S. patents for ARISTADA and/or ARISTADA INITIO and their expirations dates are as follows:

U.S. Patent No.	Product(s) Covered	Expiration Date
8,431,576	ARISTADA; ARISTADA INITIO	2030
8,796,276	ARISTADA; ARISTADA INITIO	2030
10,112,903	ARISTADA; ARISTADA INITIO	2030
10,023,537	ARISTADA	2030
9,034,867	ARISTADA	2032
9,193,685	ARISTADA	2033
9,861,699	ARISTADA	2033
9,452,131	ARISTADA	2035
9,526,726	ARISTADA	2035
10,064,859	ARISTADA	2035
10,016,415	ARISTADA INITIO	2035

In the U.S., in addition to patent protection, ARISTADA is entitled to regulatory exclusivity until October 2020, a benefit afforded to new chemical entities.

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VIVITROL and RISPERDAL CONSTA

We have a significant number of patents and certain pending patent applications covering our microsphere technology throughout the world, which, to some extent, cover VIVITROL and RISPERDAL CONSTA. The latest to expire of our patents covering VIVITROL and RISPERDAL CONSTA, expire in the U.S. in 2029 and 2023, respectively, and in the EU in 2021, and we own 13 and 4 unexpired Orange-Book listed U.S. patents covering VIVITROL and RISPERDAL CONSTA, respectively. For a discussion of legal proceedings related to certain of the patents covering VIVITROL and RISPERDAL CONSTA, see Note 16, Commitments and Contingent Liabilities in the “Notes to Consolidated Financial Statements” and “Item 3—Legal Proceedings” in this Annual Report.

INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA

Our NanoCrystal technology patent portfolio, licensed to Janssen in relation to INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA, contains a number of granted patents and pending patent applications throughout the world, including in the U.S. and in countries outside of the U.S. The latest of the patents subject to our license agreement with Janssen covering INVEGA SUSTENNA/XEPLION expires in 2030 in the U.S. and certain other countries and in 2022 in the EU. The latest to expire of the licensed patents covering INVEGA TRINZA/TREVICTA in the U.S. expired in 2017 and in the EU will expire in 2022. In addition, Janssen has other patents not subject to our license agreement, including one that covers INVEGA SUSTENNA in the U.S. and expires in 2031 and one that covers INVEGA TRINZA in the U.S. and expires in 2036. For a discussion of legal proceedings related to the patents covering INVEGA SUSTENNA, see Note 16, Commitments and Contingent Liabilities in the “Notes to Consolidated Financial Statements” and “Item 3—Legal Proceedings” in this Annual Report.

AMPYRA/FAMPYRA

Our OCR technology is protected by a patent estate including patents and patent applications filed worldwide. Some OCR patent families are product-specific (including some which are owned by our licensees), whereas others cover generic delivery platforms (e.g., different release profiles, taste masking, etc.). AMPYRA/FAMPYRA incorporates our matrix drug absorption system technology. All of the U.S. patents covering AMPYRA have expired or have been revoked. Acorda has a number of European patents covering FAMPYRA (with regulatory exclusivity in the EU until 2021), the latest of which expires in 2025. For a discussion of legal proceedings related to the patents covering AMPYRA, see Note 16, Commitments and Contingent Liabilities in the “Notes to Consolidated Financial Statements” and “Item 3—Legal Proceedings” in this Annual Report.

We also have worldwide patent protection for our Key Development Programs:

ALKS 3831

We own or have a license to U.S. and worldwide patents and patent applications that cover a class of compounds that includes the opioid modulators in ALKS 3831. In addition, we own U.S. and worldwide patents and patent applications that claim formulations and methods of treatment that cover ALKS 3831. The principal owned or licensed U.S. patents for ALKS 3831 and their expiration dates are as follows:

U.S. Patent No.	Product(s) Covered	Expiration Date
7,956,187	ALKS 3831	2021
8,252,929	ALKS 3831	2021

7,262,298	ALKS 3831	2025
8,680,112	ALKS 3831	2030
9,119,848	ALKS 3831	2031
10,005,790	ALKS 3831	2031
8,778,960	ALKS 3831	2031
9,126,977	ALKS 3831	2031
9,517,235	ALKS 3831	2031

Diroximel Fumarate (BIIB098)

We have U.S. patents and patent applications, and a number of corresponding foreign counterparts, that cover BIIB098. U.S. Patent Nos. 8,669,281 and 9,090,558, each expiring in 2033, cover compositions of or methods for BIIB098.

ALKS 4230

We have U.S. patents and patent applications, and a number of corresponding foreign counterparts, that cover ALKS 4230. U.S. Patent No. 9,359,415, expiring in 2033, covers compositions of ALKS 4230.

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Protection of Proprietary Rights and Competitive Position

We have exclusive rights through licensing agreements with third parties to issued U.S. patents, pending patent applications and corresponding patents or patent applications in countries outside the U.S, subject in certain instances to the rights of the U.S. government to use the technology covered by such patents and patent applications. Under certain licensing agreements, we are responsible for patent expenses, and we pay annual license fees and/or minimum annual royalties. In addition, under these licensing agreements, we are obligated to pay royalties on future sales of products, if any, covered by the licensed patents.

There may be patents issued to third parties that relate to our products. The manufacture, use, offer for sale, sale or import of some of our products might be found to infringe on the claims of these patents. A third party might file an infringement action against us. The cost of defending such an action is likely to be high, and we might not receive a favorable ruling. There may also be patent applications filed by third parties that relate to some of our products if issued in their present form. The patent laws of the U.S. and other countries are distinct, and decisions as to patenting, validity of patents and infringement of patents may be resolved differently in different countries.

If patents exist or are issued that cover our products, we or our licensees may not be able to manufacture, use, offer for sale, sell or import some of our products without first getting a license from the patent holder. The patent holder may not grant us a license on reasonable terms, or it may refuse to grant us a license at all. This could delay or prevent us from developing, manufacturing, selling or importing those of our products that would require the license.

We try to protect our proprietary position by filing patent applications in the U.S. and in other countries related to our proprietary technology, inventions and improvements that are important to the development of our business. Because the patent position of biopharmaceutical companies involves complex legal and factual questions, enforceability of patents cannot be predicted with certainty. The ultimate degree of patent protection that will be afforded to products and processes, including ours, in the U.S. and in other important markets, remains uncertain and is dependent upon the scope of protection decided upon by the patent offices, courts and lawmakers in these countries. Patents, if issued, may be challenged, invalidated or circumvented. Thus, any patents that we own or license from others may not provide any protection against competitors. Our pending patent applications, those we may file in the future, or those we may license from third parties, may not result in patents being issued. If issued, they may not provide us with proprietary protection or competitive advantages against competitors with similar technology. Furthermore, others may independently develop similar technologies or duplicate any technology that we have developed outside the scope of our patents. The laws of certain countries do not protect our intellectual property rights to the same extent as do the laws of the U.S.

We also rely on trade secrets, know how and technology, which are not protected by patents, to maintain our competitive position. We try to protect this information by entering into confidentiality agreements with parties that have access to it, such as our corporate partners, collaborators, licensees, employees and consultants. Any of these parties may breach the agreements and disclose our confidential information or our competitors might learn of the information in some other way. If any trade secret, know how or other technology not protected by a patent were to be disclosed to, or independently developed by, a competitor, such event could materially adversely affect our business, results of operations, cash flows and financial condition. For more information, see “Item 1A—Risk Factors.”

Our trademarks, including VIVITROL, ARISTADA and ARISTADA INITIO, are important to us and are generally covered by trademark applications or registrations in the U.S. Patent and Trademark Office and the patent or trademark offices of other countries. Products using our proprietary technologies also use trademarks that are owned by our licensees, such as the trademarks INVEGA SUSTENNA/XEPLION, INVEGA TRINZA/TREVICTA and RISPERDAL CONSTA, which are registered trademarks of Johnson & Johnson and AMPYRA and FAMPYRA, which are registered trademarks of Acorda. Trademark protection varies in accordance with local law and continues in

some countries as long as the trademark is used and in other countries as long as the trademark is registered. Trademark registrations generally are for fixed but renewable terms.

Regulatory

Regulation of Pharmaceutical Products

United States

Our current and contemplated activities, and the products and processes that result from such activities, are subject to substantial government regulation. Before new pharmaceutical products may be sold in the U.S., pre clinical studies and clinical trials of the products must be conducted and the results submitted to the FDA for approval. Clinical trial programs must determine an appropriate dose and regimen, establish substantial evidence of effectiveness and define the conditions for safe use. This is a high risk process that requires stepwise clinical studies in which the product must successfully meet pre specified endpoints.

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Pre Clinical Testing: Before beginning testing of any compounds with potential therapeutic value in human subjects in the U.S., stringent government requirements for pre clinical data must be satisfied. Pre clinical testing includes both in vitro, or in an artificial environment outside of a living organism, and in vivo, or within a living organism, laboratory evaluation and characterization of the safety and efficacy of a drug and its formulation.

Investigational New Drug Exemption: Pre clinical testing results obtained from in vivo studies in several animal species, as well as from in vitro studies, are submitted to the FDA, as part of an IND, and are reviewed by the FDA prior to the commencement of human clinical trials. The pre clinical data must provide an adequate basis for evaluating both the safety and the scientific rationale for the initial clinical studies in human volunteers.

Clinical Trials: Clinical trials involve the administration of the drug to healthy human volunteers or to patients under the supervision of a qualified investigator pursuant to an FDA reviewed protocol. Human clinical trials are typically conducted in three sequential phases, although the phases may overlap with one another and, depending upon the nature of the clinical program, a specific phase or phases may be skipped altogether. Clinical trials must be conducted under protocols that detail the objectives of the study, the parameters to be used to monitor safety, and the efficacy criteria, if any, to be evaluated. Each protocol must be submitted to the FDA as part of the IND.

- Phase 1 clinical trials—test for safety, dose tolerability, absorption, bio distribution, metabolism, excretion and clinical pharmacology and, if possible, to gain early evidence regarding efficacy.
- Phase 2 clinical trials—involve a relatively small sample of the actual intended patient population and seek to assess the efficacy of the drug for specific targeted indications, to determine dose response and the optimal dose range and to gather additional information relating to safety and potential adverse effects.
- Phase 3 clinical trials—consist of expanded, large scale studies of patients with the target disease or disorder to obtain definitive statistical evidence of the efficacy and safety of the proposed product and dosing regimen.

In the U.S., the results of the pre clinical and clinical testing of a product are then submitted to the FDA in the form of a Biologics License Application ("BLA"), or an NDA. The NDA or BLA also includes information pertaining to the preparation of the product, analytical methods, details of the manufacture of finished products and proposed product packaging and labeling. The submission of an application is not a guarantee that the FDA will find the application complete and accept it for filing. The FDA may refuse to file the application if it is not considered sufficiently complete to permit a review and will inform the applicant of the reason for the refusal. The applicant may then resubmit the application and include supplemental information.

Once an NDA or BLA is accepted for filing, the FDA has 10 months, under its standard review process, within which to review the application (for some applications, the review process is longer than 10 months). For drugs that, if approved, would represent a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications, the FDA may assign "priority review" designation and review the application within 6 months. The FDA has additional review pathways to expedite development and review of new drugs that are intended to treat serious or life threatening conditions and demonstrate the potential to address unmet medical needs, including: "Fast Track," "Breakthrough Therapy," and "Accelerated Approval." However, none of these expedited pathways ensure that a product will receive FDA approval.

As part of its review, the FDA may refer the application to an advisory committee for independent advice on questions related to the development of the drug and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee; however, historically, it has typically followed such recommendations. The FDA may determine that a Risk Evaluation and Mitigation Strategy ("REMS") is necessary to ensure that the benefits of a new product outweigh its risks. If required, a REMS may include various elements, such as publication of a medication guide, a patient package insert, a communication plan to educate health care providers of the drug's risks, limitations on who may prescribe or dispense the drug, or other measures that the FDA deems necessary to assure the safe use of the drug.

In reviewing a BLA or NDA, the FDA may grant marketing approval, or issue a complete response letter to communicate to the applicant the reasons the application cannot be approved in its then-current form and provide input on the changes that must be made before an application can be approved. Even if such additional information and data are submitted to the FDA, the FDA may ultimately decide that the BLA or NDA still does not satisfy the criteria for approval. The receipt of regulatory approval often takes a number of years, involves the expenditure of substantial resources and depends on a number of factors, including the severity of the disease in question, the availability of alternative treatments, efficacy and potential safety signals observed in pre clinical tests or clinical trials, and the risks and benefits demonstrated in clinical trials. It is impossible to predict with any certainty whether and when the FDA will grant marketing approval. Even if a product is approved, the approval may be subject to limitations based on the FDA's interpretation of the data. For example, the FDA may require, as a condition of approval, restricted distribution and use, enhanced labeling, special packaging or labeling, expedited reporting of certain adverse events, pre approval of promotional materials or restrictions on direct to consumer advertising, any of which could negatively impact the commercial success of a drug. The FDA may require a sponsor to conduct additional post marketing studies as a condition of approval to provide data on safety and effectiveness. In addition, prior to commercialization, controlled substances are subject to review and scheduling by the DEA.

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The FDA tracks information on side effects and adverse events reported during clinical studies and after marketing approval. Non compliance with safety reporting requirements may result in civil or criminal penalties. Side effects or adverse events that are identified during clinical trials can delay, impede or prevent marketing approval. Based on new safety information that emerges after approval, the FDA can mandate product labeling changes, impose a REMS or the addition of elements to an existing REMS, require new post marketing studies (including additional clinical trials), or suspend or withdraw approval of the product.

If we seek to make certain types of changes to an approved product, such as adding a new indication, making certain manufacturing changes, or changing manufacturers or suppliers of certain ingredients or components, the FDA will need to review and approve such changes in advance. In the case of a new indication, we are required to demonstrate with additional clinical data that the product is safe and effective for the new intended use. Such regulatory reviews can result in denial or modification of the planned changes, or requirements to conduct additional tests or evaluations that can substantially delay or increase the cost of the planned changes.

In addition, the FDA regulates all advertising and promotional activities for products under its jurisdiction. A company can make only those claims relating to safety and efficacy that are consistent with FDA regulation and guidance. However, physicians may prescribe legally available drugs for uses that are not described in the drug's labeling. Such off label uses are common across certain medical specialties and often reflect a physician's belief that the off label use is the best treatment for a particular patient. The FDA does not regulate the behavior of physicians in their choice of treatments, but the FDA regulations do impose stringent restrictions on manufacturers' communications regarding off label uses. Failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA and the U.S. Department of Justice, corrective advertising and the full range of civil and criminal penalties available to the FDA and the U.S. Department of Justice.

Controlled Substances Act: The DEA regulates pharmaceutical products that are controlled substances. Controlled substances are those drugs that appear on one of the five schedules promulgated and administered by the DEA under the Controlled Substances Act (the "CSA"). The CSA governs, among other things, the inventory, distribution, recordkeeping, handling, security and disposal of controlled substances. Pharmaceutical products that act on the CNS are often evaluated for abuse potential; a product that is then classified as a controlled substance must undergo scheduling by the DEA, which is a separate process that may delay the commercial launch of a pharmaceutical product even after FDA approval of the NDA for such product. Companies with a scheduled pharmaceutical product are subject to periodic and ongoing inspections by the DEA and similar state drug enforcement authorities to assess ongoing compliance with the DEA's regulations. Any failure to comply with these regulations could lead to a variety of sanctions, including the revocation, or a denial of renewal, of any DEA registration and injunctions, or civil or criminal penalties.

Outside the United States

Certain of our products are commercialized by our licensees in numerous jurisdictions outside the U.S. Most of these jurisdictions have product approval and post approval regulatory processes that are similar in principle to those in the U.S. In Europe, there are several tracks for marketing approval, depending on the type of product for which approval is sought. Under the centralized procedure, a company submits a single application to the EMA. The marketing application is similar to the NDA in the U.S. and is evaluated by the Committee for Medicinal Products for Human Use ("CHMP"), the expert scientific committee of the EMA. If the CHMP determines that the marketing application fulfills the requirements for quality, safety, and efficacy, it will submit a favorable opinion to the European Commission ("EC"). The CHMP opinion is not binding, but is typically adopted by the EC. A marketing application approved by the EC is valid in all member states.

In addition to the centralized procedure, Europe also has: (i) a nationalized procedure, which requires a separate application to, and approval determination by, each country; (ii) a decentralized procedure, whereby applicants submit identical applications to several countries and receive simultaneous approval; and (iii) a mutual recognition procedure, where applicants submit an application to one country for review and other countries may accept or reject the initial decision. Regardless of the approval process employed, various parties share responsibilities for the monitoring, detection and evaluation of adverse events post approval, including national authorities, the EMA, the EC and the marketing authorization holder.

Good Manufacturing Processes

The FDA, the EMA, the competent authorities of the EU member states and other regulatory agencies regulate and inspect equipment, facilities and processes used in the manufacturing of pharmaceutical and biologic products prior to approving a product. If, after receiving clearance from regulatory agencies, a company makes a material change in manufacturing equipment, location or process, additional regulatory review and approval may be required. Companies also must adhere to cGMP and product specific regulations enforced by the FDA following product approval. The FDA, the EMA and other regulatory agencies also conduct regular, periodic visits to re inspect equipment, facilities and processes following the initial approval of a product. If, as a result of these inspections, it is determined that our equipment, facilities or processes do not comply with applicable regulations and conditions of product approval, regulatory agencies may seek civil, criminal or administrative sanctions and/or remedies against us, including the suspension of our manufacturing operations.

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Good Clinical Practices

The FDA, the EMA and other regulatory agencies promulgate regulations and standards, commonly referred to as Good Clinical Practices ("GCP"), for designing, conducting, monitoring, auditing and reporting the results of clinical trials to ensure that the data and results are accurate and that the trial participants are adequately protected. The FDA, the EMA and other regulatory agencies enforce GCP through periodic inspections of trial sponsors, principal investigators, trial sites, contract research organizations ("CROs") and institutional review boards. If our studies fail to comply with applicable GCP, patient safety and well-being could be impacted, the clinical data generated in our clinical trials may be deemed unreliable, and relevant regulatory agencies may require us to perform additional clinical trials before approving our marketing applications. Noncompliance can also result in civil or criminal sanctions. We rely on third parties, including CROs, to carry out many of our clinical trial related activities. Failure of such third parties to comply with GCP can likewise result in rejection of our clinical trial data or other sanctions.

Hatch Waxman Act

Under the U.S. Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch Waxman Act"), Congress created an abbreviated FDA review process for generic versions of pioneer, or brand name, drug products. The law also provides incentives by awarding, in certain circumstances, non patent related marketing exclusivities to pioneer drug manufacturers. Newly approved drug products and changes to the conditions of use of approved products may benefit from periods of non patent related marketing exclusivity in addition to any patent protection the drug product may have. The Hatch Waxman Act provides five years of new chemical entity ("NCE") marketing exclusivity to the first applicant to gain approval of an NDA for a product that contains an active ingredient, known as the active drug moiety, not found in any other approved product. The FDA is prohibited from accepting any abbreviated NDA ("ANDA") for a generic drug or 505(b)(2) application referencing the NCE for five years from the date of approval of the NCE, or four years in the case of an ANDA or 505(b)(2) application containing a patent challenge. A 505(b)(2) application is an NDA wherein the applicant relies, in part, on data and the FDA's findings of safety and efficacy from studies not conducted by or for it and for which the applicant has not obtained a right of reference. Hatch-Waxman Act exclusivities will not prevent the submission or approval of a full NDA (e.g., under 505(b)(1)), as opposed to an ANDA or 505(b)(2) application, for any drug, including, for example, a drug with the same active ingredient, dosage form, route of administration, strength and conditions of use.

The Hatch Waxman Act also provides three years of exclusivity for applications containing the results of new clinical investigations, other than bioavailability studies, essential to the FDA's approval of new uses of approved products, such as new indications, dosage forms, strengths, or conditions of use. However, this exclusivity only protects against the approval of ANDAs and 505(b)(2) applications for the protected use and will not prohibit the FDA from accepting or approving ANDAs or 505(b)(2) applications for other products containing the same active ingredient.

The Hatch Waxman Act requires NDA applicants and NDA holders to provide certain information about patents related to the drug for listing in the FDA's Approved Drugs Product List, commonly referred to as the Orange Book. ANDA and 505(b)(2) applicants must then certify regarding each of the patents listed with the FDA for the reference product. A certification that a listed patent is invalid or will not be infringed by the marketing of the applicant's product is called a "Paragraph IV certification." If the ANDA or 505(b)(2) applicant provides such a notification of patent invalidity or noninfringement, then the FDA may accept the ANDA or 505(b)(2) application four years after approval of the NDA for an NCE. If a Paragraph IV certification is filed and the ANDA or 505(b)(2) application has been accepted as a reviewable filing by the FDA, the ANDA or 505(b)(2) applicant must then, within 20 days, provide notice to the NDA holder and patent owner stating that the application has been submitted and providing the factual and legal basis for the applicant's opinion that the patent is invalid or not infringed. The NDA holder or patent owner may file suit against the ANDA or 505(b)(2) applicant for patent infringement. If this is done within 45 days of receiving notice of the Paragraph IV certification, a one time, 30 month stay of the FDA's ability to approve the ANDA

or 505(b)(2) application is triggered. The 30 month stay begins at the end of the NDA holder's data exclusivity period, or, if data exclusivity has expired, on the date that the patent holder is notified. The FDA may approve the proposed product before the expiration of the 30 month stay if a court finds the patent invalid or not infringed, or if the court shortens the period because the parties have failed to cooperate in expediting the litigation.

Sales and Marketing

We are subject to various U.S. federal and state laws pertaining to healthcare fraud and abuse, including anti kickback laws and false claims laws. Anti kickback laws make it illegal for a prescription drug manufacturer to solicit, offer, receive, or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug. Due to the broad scope of the U.S. statutory provisions, the general absence of guidance in the form of regulations, and few court decisions addressing industry practices, it is possible that our practices might be challenged under anti kickback or similar laws. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented, for payment to third party payers (including Medicare and Medicaid) claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed or claims for medically unnecessary items or services. Activities relating to the sale and marketing of our products may be subject to scrutiny under these laws. Violations of fraud and abuse laws may be punishable by criminal and/or civil

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sanctions, including fines and civil monetary penalties, as well as the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid). In addition, federal and state authorities are paying increased attention to enforcement of these laws within the pharmaceutical industry and private individuals have been active in alleging violations of the laws and bringing suits on behalf of the government under the federal civil False Claims Act. If we were subject to allegations concerning, or were convicted of violating, these laws, our business could be harmed. See "Item 1A—Risk Factors" and specifically those sections entitled "—If we fail to comply with the extensive legal and regulatory requirements affecting the healthcare industry, we could face increased costs, penalties and a loss of business," "—Revenues generated by sales of our products depend on the availability of reimbursement from third party payers, and a reduction in payment rate or reimbursement or an increase in our financial obligation to governmental payers could result in decreased sales of our products and decreased revenues" and "—The commercial use of our products may cause unintended side effects or adverse reactions, or incidents of misuse may occur, which could adversely affect our business and share price."

Laws and regulations have been enacted by the federal government and various states to regulate the sales and marketing practices of pharmaceutical manufacturers. The laws and regulations generally limit financial interactions between manufacturers and healthcare providers and require disclosure to the government and public of such interactions. The laws include federal "sunshine", or open payments, provisions enacted in 2010 as part of the comprehensive federal healthcare reform legislation and supplemented as part of the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act. Such provisions apply to pharmaceutical manufacturers with products reimbursed under certain government programs and require those manufacturers to disclose annually to the federal government (for re disclosure to the public) certain payments made to, or at the request of, or on behalf of, physicians or to teaching hospitals and, commencing for information to be submitted as of January 1, 2022, certain payments made to physicians assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and certified nurse-midwives. Certain state laws also require disclosure of pharmaceutical pricing information and marketing expenditures. Given the ambiguity found in many of these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent federal and state laws and regulations.

Pricing and Reimbursement

United States

In the U.S., sales of our products, including those sold by our licensees, and our ability to generate revenues on such sales are dependent, in significant part, on the availability and level of reimbursement from third party payers such as state and federal governments, including Medicare and Medicaid, managed care providers and private insurance plans. Third party payers are increasingly challenging the prices charged for medical products and examining the medical necessity and cost effectiveness of medical products, in addition to their safety and efficacy.

Medicaid is a joint federal and state program that is administered by the states for low income and disabled beneficiaries. Under the Medicaid rebate program, we are required to pay a rebate for each unit of product reimbursed by the state Medicaid programs. The amount of the rebate for each product is set by law as the greater of 23.1% of average manufacturer price ("AMP") or the difference between AMP and the best price available from us to any commercial or non federal governmental customer. The rebate amount must be adjusted upward where the AMP for a product's first full quarter of sales, when adjusted for increases in the Consumer Price Index—Urban, is less than the AMP for the current quarter, with this difference being the amount by which the rebate is adjusted upwards. The rebate amount is required to be recomputed each quarter based on our report of current AMP and best price for each of our products to the Centers for Medicare & Medicaid Services ("CMS"). The terms of our participation in the rebate program imposes a requirement for us to report revisions to AMP or best price within a period not to exceed 12 quarters from the quarter in which the data was originally due. Any such revisions could have the impact of increasing

or decreasing our rebate liability for prior quarters, depending on the direction of the revision. In addition, if we were found to have knowingly submitted false information to the government, the statute provides for civil monetary penalties per item of false information in addition to other penalties available to the government. Medicare is a federal program that is administered by the federal government that covers individuals age 65 and over as well as those with certain disabilities. Medicare Part B pays physicians who administer our products under a payment methodology using average sales price ("ASP") information. Manufacturers, including us, are required to provide ASP information to the CMS on a quarterly basis. This information is used to compute Medicare payment rates, with rates for Medicare Part B drugs outside the hospital outpatient setting and in the hospital outpatient setting consisting of ASP plus a specified percentage. These rates are adjusted periodically. If a manufacturer is found to have made a misrepresentation in the reporting of ASP, the statute provides for civil monetary penalties for each misrepresentation and for each day in which the misrepresentation was applied.

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Medicare Part D provides coverage to enrolled Medicare patients for self administered drugs (i.e. drugs that do not need to be injected or otherwise administered by a physician) and certain physician-administered drugs reimbursed under a pharmacy benefit. Medicare Part D also covers the prescription drug benefit for dual eligible beneficiaries. Medicare Part D is administered by private prescription drug plans approved by the U.S. government and each drug plan establishes its own Medicare Part D formulary for prescription drug coverage and pricing, which the drug plan may modify from time to time. The prescription drug plans negotiate pricing with manufacturers and may condition formulary placement on the availability of manufacturer discounts. Except for dual eligible Medicare Part D beneficiaries who qualify for low income subsidies, manufacturers, including us, are required to provide a fifty percent (50%) discount on our brand name prescription drugs utilized by Medicare Part D beneficiaries when those beneficiaries reach the coverage gap in their drug benefits; the Bipartisan Budget Act of 2018, signed into law on February 9, 2018, increased this discount percentage on brand name prescription drugs to seventy percent (70%) starting in 2019.

The availability of federal funds to pay for our products under the Medicaid Drug Rebate Program and Medicare Part B requires that we extend discounts to certain purchasers under the Public Health Services ("PHS") pharmaceutical pricing program. Purchasers eligible for discounts include a variety of community health clinics, other entities that receive health services grants from PHS, and hospitals that serve a disproportionate share of financially needy patients.

We also make our products available for purchase by authorized users of the Federal Supply Schedule ("FSS") of the General Services Administration pursuant to our FSS contract with the Department of Veterans Affairs. Under the Veterans Health Care Act of 1992 (the "VHC Act"), we are required to offer deeply discounted FSS contract pricing to four federal agencies: the Department of Veterans Affairs; the Department of Defense; the Coast Guard; and the PHS (including the Indian Health Service), in order for federal funding to be made available for reimbursement of any of our products by such federal agencies and certain federal grantees. Coverage under Medicaid, the Medicare Part B program and the PHS pharmaceutical pricing program is also conditioned upon FSS participation. FSS pricing is negotiated periodically with the Department of Veterans Affairs. FSS pricing is intended not to exceed the price that we charge our most favored non federal customer for a product. In addition, prices for drugs purchased by the Department of Veterans Affairs, Department of Defense (including drugs purchased by military personnel and dependents through the TriCare retail pharmacy program), Coast Guard and PHS are subject to a cap on pricing equal to 76% of the non federal average manufacturer price ("non FAMP"). An additional discount applies if non FAMP increases more than inflation (measured by the Consumer Price Index—Urban). In addition, if we are found to have knowingly submitted false information to the government, the VHC Act provides for civil monetary penalties per false item of information in addition to other penalties available to the government.

In addition, on January 21, 2016, CMS released the final Medicaid covered outpatient drug regulation, which became effective on April 1, 2016. This regulation implements those changes made by the Patient Protection and Affordable Care Act (the "PPACA") to the Medicaid drug rebate statute in 2010 and addresses a number of other issues with respect to the Medicaid program, including, but not limited to, the eligibility and calculation methodologies for AMP and best price, and the expansion of Medicaid rebate liability to include Medicaid managed care organizations. The final Medicaid covered outpatient drug regulation established two calculation methodologies for AMP: one for drugs generally dispensed through retail community pharmacies ("RCP") and one for so-called "5i drugs" (inhaled, infused, instilled, implanted or injectable drugs) "not generally dispensed" through RCPs. The regulation further made clear that 5i drugs would qualify as "not generally dispensed" and, therefore, able to use the alternative AMP calculation, if not more than thirty percent (30%) of their sales were to RCPs or to wholesalers for RCPs. The primary difference between the two AMP calculations is the requirement to exclude from AMP, for those qualifying 5i drugs not generally dispensed through RCPs, certain payments, rebates and discounts related to sales to non-RCPs; such exclusion often leads to a lower AMP. The decision of which AMP calculation a product is eligible to use must be made and applied on a monthly basis based on the percentage of sales of such product to RCPs or to wholesalers for

RCPs.

The U.S. federal and state governments regularly consider reforming healthcare coverage and lessening healthcare costs. Such reforms may include price controls, value-based pricing and changes to the coverage and reimbursement of our products, which may have a significant impact on our business. For example, on January 31, 2019, the Department of Health and Human Services (HHS) released a notice of proposed rulemaking as part of ongoing administration drug pricing reform efforts that would modify a regulatory provision that had previously protected certain pharmaceutical manufacturer rebates from criminal prosecution and financial penalties under the federal Anti-Kickback Statute and that would add new regulatory safe harbors for certain price reductions passed through to dispensing pharmacies and payments to pharmacy benefit managers. In addition, emphasis on managed care in the U.S. has increased and we expect will continue to increase the pressure on drug pricing. Private insurers regularly seek to manage drug cost and utilization by implementing coverage and reimbursement limitations through means including, but not limited to, formularies, increased out of pocket obligations and various prior authorization requirements. Even if favorable coverage and reimbursement status is attained for one or more products for which we have received regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

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Outside the United States

Within the EU, products are paid for by a variety of payers, with governments being the primary source of payment. Governments may determine or influence reimbursement of products. Governments may also set prices or otherwise regulate pricing. Negotiating prices with governmental authorities can delay commercialization of products. Governments may use a variety of cost containment measures to control the cost of products, including price cuts, mandatory rebates, value based pricing and reference pricing (i.e. referencing prices in other countries and using those reference prices to set a price). Recent budgetary pressures in many EU countries are causing governments to consider or implement various cost containment measures, such as price freezes, increased price cuts and rebates, and expanded generic substitution and patient cost sharing. If budget pressures continue, governments may implement additional cost containment measures.

Other Regulations

Foreign Corrupt Practices Act: We are subject to the U.S. Foreign Corrupt Practices Act (the "FCPA"), which prohibits U.S. corporations and their representatives from paying, offering to pay, promising, authorizing, or making payments of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. In many countries, the healthcare professionals with whom we regularly interact may meet the FCPA's definition of a foreign government official. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect their transactions and to devise and maintain an adequate system of internal accounting controls.

Environmental, Health and Safety Laws: Our operations are subject to complex and increasingly stringent environmental, health and safety laws and regulations in the countries where we operate and, in particular, where we have manufacturing facilities, namely the U.S. and Ireland. Environmental and health and safety authorities in the relevant jurisdictions, including the Environmental Protection Agency and the Occupational Safety and Health Administration in the U.S. and the Environmental Protection Agency and the Health and Safety Authority in Ireland, administer laws which regulate, among other matters, the emission of pollutants into the air (including the workplace), the discharge of pollutants into bodies of water, the storage, use, handling and disposal of hazardous substances, the exposure of persons to hazardous substances, and the general health, safety and welfare of employees and members of the public. In certain cases, these laws and regulations may impose strict liability for pollution of the environment and contamination resulting from spills, disposals or other releases of hazardous substances or waste and/or any migration of such hazardous substances or waste. Costs, damages and/or fines may result from the presence, investigation and remediation of contamination at properties currently or formerly owned, leased or operated by us and/or off site locations, including where we have arranged for the disposal of hazardous substances or waste. In addition, we may be subject to third party claims, including for natural resource damages, personal injury and property damage, in connection with such contamination.

The General Data Protection Regulation ("GDPR"): The GDPR came into force on May 25, 2018 and replaced the previous European Union ("EU") Data Protection Directive (95/46). The GDPR, which governs the processing of personal data (including personal health data), applies to the Company and any of its subsidiaries that are established in the EU as well as any of its subsidiaries that are established outside the EU to the extent that they process personal data relating to clinical trial participants in the EU. The GDPR imposes significant obligations on controllers and processors of personal data, including, as compared to the prior directive, higher standards for obtaining consent from individuals to process their personal data, more robust notification requirements to individuals about the processing of their personal data, a strengthened individual data rights regime, mandatory data breach notifications, limitations on the retention of personal data, increased requirements pertaining to health data, and strict rules and restrictions on the transfer of personal data outside of the EU, including to the U.S. The GDPR also imposes additional obligations on,

and required contractual provisions to be included in, contracts between companies subject to the GDPR and their third-party processors that relate to the processing of personal data. The GDPR allows EU member states to make additional laws and regulations further limiting the processing of genetic, biometric or health data..

Other Laws: We are subject to a variety of financial disclosure, securities trading regulations and governmental regulations as an Irish-incorporated public company in the U.S., including laws relating to the oversight activities of the Securities and Exchange Commission ("SEC"), the Irish Companies Act 2014, and the regulations of the Nasdaq, on which our shares are traded. We are also subject to various laws, regulations and recommendations relating to safe working conditions, laboratory practices, the experimental use of animals, and the purchase, storage, movement, import and export and use and disposal of hazardous or potentially hazardous substances used in connection with our research work.

Employees

As of February 4, 2019, we had approximately 2,300 full time employees. A significant number of our management and professional employees have prior experience with pharmaceutical, biopharmaceutical or medical product companies. We believe that we have been successful in attracting skilled and experienced scientific and senior management personnel; however, competition for such personnel is intense. None of our employees is covered by a collective bargaining agreement. We consider our relations with our employees to be good.

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Available Information and Website Disclosure

Our principal executive offices are located at Connaught House, 1 Burlington Road, Dublin 4, Ireland. Our telephone number is +353 1 772 8000 and our website address is www.alkermes.com. Information that is contained in and can be accessed through, our website is not incorporated into, and does not form a part of, this Annual Report. We make available free of charge through the Investors section of our website our Annual Reports on Form 10 K, Quarterly Reports on Form 10 Q, Current Reports on Form 8 K and all amendments to those reports as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. We also make available on our website (i) the charters for the standing committees of our board of directors, including the Audit and Risk Committee, Compensation Committee, and Nominating and Corporate Governance Committee, and (ii) our Code of Business Conduct and Ethics governing our directors, officers and employees. We intend to disclose on our website any amendments to, or waivers from, our Code of Business Conduct and Ethics that are required to be disclosed pursuant to the rules of the SEC.

From time to time, we may use our website to distribute material information. Our financial and other material information is routinely posted to and accessible on the Investors section of our website, available at www.alkermes.com. Investors are encouraged to review the Investors section of our website because we may post material information on that site that is not otherwise disseminated by us. Information that is contained in and can be accessed through our website is not incorporated into, and does not form a part of, this Annual Report.

Item 1A. Risk Factors

You should consider carefully the risks described below in addition to the financial and other information contained in this Annual Report, including the matters addressed under the caption “Cautionary Note Concerning Forward-Looking Statements.” If any events described by the following risks actually occur, they could materially adversely affect our business, financial condition, cash flows or results of operations. This could cause the market price of our ordinary shares to decline.

We rely heavily on our licensees in the commercialization and continued development of products from which we receive revenue; and if our licensees are not effective, our revenues could be materially adversely affected.

Our arrangements with licensees are critical to bringing products using our proprietary technologies and from which we receive manufacturing and/or royalty revenue to the market and successfully commercializing them. We rely on these licensees in various respects, including commercializing such products; providing funding for development programs and conducting pre-clinical testing and clinical trials with respect to new formulations or other development activities for such products; and managing the regulatory approval process.

The revenues that we receive from manufacturing fees and royalties depend primarily upon the success of our licensees, and particularly Janssen, Acorda and Biogen, in commercializing certain products. Janssen is responsible for the commercialization of RISPERDAL CONSTA, INVEGA SUSTENNA/XEPLION, and INVEGA TRINZA/TREVICTA, and, in Russia and the CIS, VIVITROL. Acorda and Biogen are responsible for commercializing AMPYRA and FAMPYRA, respectively. We have no involvement in the commercialization efforts for these and other products sold by third parties to which we have licensed our proprietary technology. Our revenues may fall below our expectations, the expectations of our licensees or those of investors, which could have a material adverse effect on our results of operations and the market price of our ordinary shares. Such revenues will depend on numerous factors, many of which are outside our control.

Our licensees may also choose to use their own or other technology to develop an alternative product and withdraw their support of our product, or to compete with our jointly developed product. In addition, ARISTADA competes

directly with RISPERDAL CONSTA, INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA, products from which we receive manufacturing and/or royalty revenue. Disputes may also arise between us and a licensee and may involve the ownership of technology developed under a license or other issues arising out of collaborative agreements. Such a dispute could delay the related program or result in expensive arbitration or litigation, which may not be resolved in our favor.

In addition, most of our licensees can terminate their agreements with us without cause, and we cannot guarantee that any of these relationships will continue. Failure to make or maintain these arrangements or a delay in, or failure of, a licensee's performance, or factors that may affect a licensee's sales, may materially adversely affect our business, financial condition, cash flows and results of operations.

We receive substantial revenues from our key products.

We depend substantially upon continued sales of INVEGA SUSTENNA/XEPLION, INVEGA TRINZA/TREVICTA and RISPERDAL CONSTA by Janssen, upon continued sales of FAMPYRA by Biogen, and upon our continued sales of VIVITROL and ARISTADA. Any significant negative developments relating to these products, or to our licensee relationships, could have a material adverse effect on our business, results of operations, cash flows and financial condition.

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Our revenues may be lower than expected as a result of failure by the marketplace to accept our products or for other factors.

We cannot be assured that our products will be, or will continue to be, accepted in the U.S. or in any markets outside the U.S. or that sales of our products will not decline or cease in the future. A number of factors may cause revenues from sales of our products to grow at a slower than expected rate, or even to decrease or cease, including:

- the perception of physicians and other members of the healthcare community as to our products' safety and efficacy relative to that of competing products and the willingness or ability of physicians and other members of the healthcare community to prescribe or dispense, and patients to use, our products, including those that may be scheduled by the DEA (if and when approved);
- unfavorable publicity concerning us or our products, similar classes of drugs or the industry generally;
- the cost-effectiveness of our products;
- patient and physician satisfaction with our products;
- the successful manufacture of our products on a timely and cost-effective basis;
- the cost and availability of raw materials necessary for the manufacture of our products;
- the size of the markets for our products;
- reimbursement policies of government and third-party payers;
- the introduction, availability and acceptance of competing treatments, including treatments marketed and sold by our licensees;
- the reaction of companies that market competitive products;
- adverse event information relating to our products or to similar classes of drugs;
- changes to the product labels of our products, or of products within the same drug classes, to add significant warnings or restrictions on use;
- our continued ability to access third parties to vial, package and/or distribute our products on acceptable terms;
- the unfavorable outcome of investigations, litigation or other legal proceedings, including government investigations regarding VIVITROL, securities litigation relating to VIVITROL and ALKS 5461, and litigation or other proceedings before the U.S. Patent and Trademark Office's (the "USPTO") Patent Trial and Appeal Board (the "PTAB"), including so-called "Paragraph IV" litigation relating to INVEGA SUSTENNA and AMPYRA, inter partes reviews ("IPR") relating to VIVITROL, opposition proceedings in the EU relating to RISPERDAL CONSTA and any other litigation related to any of our products;
- regulatory developments related to the manufacture or continued use of our products, including the issuance of a REMS by the FDA;
- the extent and effectiveness of the sales and marketing and distribution support our products receive, including from our licensees;
- our licensees' decisions as to the timing and volume of product orders and product shipments, the timing of product launches, and product pricing and discounting;
- disputes with our licensees relating to the marketing and sale of products from which we receive revenue;
- exchange rate valuations and fluctuations;
- global political changes and/or instability, including the expected exit of the United Kingdom from the European Union (commonly referred to as "Brexit"), and any related changes in applicable laws and regulations, that may impact resources and markets for our products outside of the U.S.; and
- any other material adverse developments with respect to the commercialization of our products.

These and other factors could materially adversely affect our revenues, financial condition, cash flows and results of operations.

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The FDA or other regulatory agencies may not approve our products or may delay approval.

We must obtain government approvals before marketing or selling our products in the U.S. and in jurisdictions outside the U.S. The FDA, DEA (to the extent a product is a controlled substance), and comparable regulatory agencies in other countries, impose substantial and rigorous requirements for the development, production and commercial introduction of drug products. These include pre-clinical, laboratory and clinical testing procedures, sampling activities, clinical trials and other costly and time-consuming procedures. Satisfaction of the requirements of the FDA and of other regulatory agencies typically takes a significant number of years and can vary substantially based upon the type, complexity and novelty of the product.

In addition, regulation is not static, and regulatory agencies, including the FDA, evolve in their staff, interpretations and practices and may impose more stringent requirements than currently in effect, which may adversely affect our planned drug development and/or our commercialization efforts. The approval procedure and the time required to obtain approval also varies among countries. Regulatory agencies may have varying interpretations of the same data, and approval by one regulatory agency does not ensure approval by regulatory agencies in other jurisdictions. In addition, the FDA or regulatory agencies outside the U.S. may choose not to communicate with or update us during clinical testing and regulatory review periods. The ultimate decision by the FDA or other regulatory agencies regarding drug approval may not be consistent with prior communications.

This product approval process can last many years, be very costly and still be unsuccessful. Regulatory approval by the FDA or regulatory agencies outside the U.S. can be delayed, limited or not granted at all for many reasons, including:

- a product may not demonstrate safety and efficacy for each target indication in accordance with the FDA's or other regulatory agencies' standards;
- data from pre-clinical testing and clinical trials may be interpreted by the FDA or other regulatory agencies in different ways than we or our licensees interpret it;
- the FDA or other regulatory agencies may not agree with our or our licensees' regulatory approval strategies, components of our or our licensees' filings, such as clinical trial designs, conduct and methodologies, or the sufficiency of our or our licensees' submitted data;
- the FDA or other regulatory agencies might not approve our or our licensees' manufacturing processes or facilities;
- the FDA or other regulatory agencies may not approve accelerated development timelines for our products;
- the failure of our clinical investigational sites and the records kept at such sites, including the clinical trial data, to be in compliance with the FDA's GCP, or EU legislation governing GCP, including the failure to pass FDA, EMA or EU member state inspections of clinical trials;
- the FDA or other regulatory agencies may change their approval policies or adopt new regulations; and
- adverse medical events during the trials could lead to requirements that trials be repeated or extended, or that a program be terminated or placed on clinical hold, even if other studies or trials relating to the program are successful.

In addition, disruptions at the FDA and other regulatory agencies that are unrelated to our company or our products could also cause delays to the regulatory approval process for our products. For example, over the last several years, including in December 2018 and January 2019, the U.S. government has shut down several times and certain regulatory agencies, including the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions.

Failure to obtain regulatory approval for products will prevent their commercialization. Any delay in obtaining regulatory approval for products could adversely affect our ability to successfully commercialize such products. In addition, share prices have declined significantly in certain instances where companies have failed to obtain FDA

approval of a product or where the timing of FDA approval is delayed. If the FDA's or any other regulatory agency's response to any application for approval is delayed or not favorable for any of our products, our share price could decline significantly and could materially adversely affect our business, financial condition, cash flows and results of operations.

Clinical trials for our products are expensive, may take several years to complete, and their outcomes are uncertain.

Before obtaining regulatory approvals for the commercial sale of any products, we or our licensees must demonstrate, through pre-clinical testing and clinical trials, that our products are safe and effective for use in humans. Conducting clinical trials is a lengthy, time-consuming and expensive process. We have incurred, and we will continue to incur, substantial expense for pre-clinical testing and clinical trials.

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Our pre-clinical and clinical development efforts may not be successfully completed. Completion of clinical trials may take several years or more. The length of time can vary substantially with the type, complexity, novelty and intended use of the product. The commencement and rate of completion of clinical trials may be delayed by many factors, including:

- the potential delay by a partner in beginning a clinical trial;
- the failure of third-party contract research organizations ("CROs") and other third-party service providers and independent clinical investigators to manage and conduct the trials, to perform their oversight of the trials or to meet expected deadlines;
- the inability to recruit clinical trial participants at the expected rate;
- the inability to follow patients adequately after treatment;
- unforeseen safety issues;
- the inability to manufacture or obtain sufficient quantities of materials used for clinical trials; and
- unforeseen governmental or regulatory issues or concerns, including those of the FDA, DEA and other regulatory agencies.

In addition, we are currently conducting and enrolling patients in clinical studies in a number of countries where our experience is more limited. We depend on independent clinical investigators, CROs and other third-party service providers and our collaborators in the conduct of clinical trials for our products and in the accurate reporting of results from such clinical trials. We rely heavily on these parties for successful execution of our clinical trials but do not control many aspects of their activities. For example, while the investigators are not our employees, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Third parties may not complete activities on schedule or may not conduct our clinical trials in accordance with regulatory requirements or our stated protocols.

The outcome of our clinical trials is uncertain. The results from pre-clinical testing and early clinical trials often have not predicted results of later clinical trials. A number of products have shown promising results in early clinical trials but subsequently failed to establish sufficient safety and efficacy data in later clinical trials to obtain necessary regulatory approvals.

If a product fails to demonstrate safety and efficacy in clinical trials, or if third parties fail to conduct clinical trials in accordance with their obligations, the development, approval and commercialization of our products may be delayed or prevented, and such events could materially adversely affect our business, financial condition, cash flows and results of operations.

We are subject to risks related to the manufacture of our products.

The manufacture of pharmaceutical products is a highly complex process in which a variety of difficulties may arise from time to time including, but not limited to, product loss due to material failure, equipment failure, vendor error, operator error, labor shortages, inability to obtain material, equipment or transportation, physical or electronic security breaches, natural disasters and many other factors. Problems with manufacturing processes could result in product defects or manufacturing failures, which could require us to delay shipment of products or recall products previously shipped, or could impair our ability to expand into new markets or supply products in existing markets. We may not be able to resolve any such problems in a timely fashion, if at all.

We rely solely on our manufacturing facility in Wilmington, Ohio for the manufacture of RISPERDAL CONSTA, VIVITROL, ARISTADA, ARISTADA INITIO and certain of our other development products. We rely on our manufacturing facility in Athlone, Ireland for the manufacture of AMPYRA (including the authorized generic version of AMPYRA), FAMPYRA and some of our other products using our NanoCrystal and OCR technologies.

Due to regulatory and technical requirements, we have limited ability to shift production among our facilities or to outsource any part of our manufacturing to third parties. Any such shift of production among our facilities or transition of our manufacturing processes to a third party could take a significant amount of time and money and may not be successful.

Our manufacturing facilities also require specialized personnel and are expensive to operate and maintain. Any delay in the regulatory approval or market launch of products, or suspension of the sale of our products, manufactured in our facilities, may cause operating losses as we continue to operate these facilities and retain specialized personnel. In addition, any interruption in manufacturing could result in delays in meeting contractual obligations and could damage our relationships with our licensees, including the loss of manufacturing and supply rights.

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We rely on third parties to provide services in connection with the manufacture and distribution of our products.

We rely on third parties for the timely supply of specified raw materials, equipment, contract manufacturing, formulation and packaging services, storage and product distribution services, customer service activities and product returns processing. These third parties must comply with federal, state and local regulations applicable to their business, including FDA and, as applicable, DEA regulations. Although we actively manage these third-party relationships to ensure continuity, quality and compliance with regulations, some events beyond our control could result in the complete or partial failure of these goods and services. Any such failure could materially adversely affect our business, financial condition, cash flows and results of operations.

The manufacture of products and product components, including the procurement of bulk drug product and other materials used in the manufacture of products, and packaging, storage and distribution of our products, requires successful coordination among us and multiple third-party providers. For example, we are responsible for the entire supply chain for ARISTADA, ARISTADA INITIO and VIVITROL, up to the sale of final product and including the sourcing of key raw materials and active pharmaceutical agents from third parties. Issues with our third-party providers, including our inability to coordinate these efforts, lack of capacity available at such third-party providers or any other problems with the operations of these third-party providers, could require us to delay shipment of saleable products, recall products previously shipped or could impair our ability to supply products at all. This could increase our costs, cause us to lose revenue or market share and damage our reputation and have a material adverse effect on our business, financial condition, cash flows and results of operations.

We endeavor to qualify and register new vendors and to develop contingency plans so that production is not impacted by issues associated with third-party providers. Nonetheless, our business could be materially and adversely affected by issues associated with third-party providers.

We are also dependent in certain cases on third parties to manufacture products. Where the manufacturing rights to the products using our technologies are granted to, or retained by, our third-party licensee (for example, in the cases of INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA) or approved sub-licensee, we have no control over the manufacturing, supply or distribution of the product. Supply or manufacturing issues encountered by such licensees or sublicenses could materially and adversely affect sales of such products from which we receive revenue, and our business, financial condition, cash flows and results of operations.

If we or our third-party providers fail to meet the stringent requirements of governmental regulation in the manufacture of our products, we could incur substantial remedial costs and a reduction in sales and/or revenues.

We and our third-party providers are generally required to comply with cGMP regulations and other applicable foreign standards in the manufacture of our products. In addition, in the U.S., the DEA and state-level agencies heavily regulate the manufacturing, holding, processing, security, recordkeeping and distribution of substances, including controlled substances. Our products that are scheduled by the DEA as controlled substances make us subject to the DEA's regulations. We are subject to unannounced inspections by the FDA, the DEA and comparable state and foreign agencies in other jurisdictions to confirm compliance with all applicable laws. Any changes of suppliers or modifications of methods of manufacturing require amending our application to the FDA or other regulatory agencies, and ultimate amendment acceptance by such agencies, prior to release of product to the applicable marketplace. Our inability or the inability of our third-party providers to demonstrate ongoing cGMP or other regulatory compliance could require us to withdraw or recall products and interrupt clinical and commercial supply of our products. Any delay, interruption or other issues that may arise in the manufacture, formulation, packaging or storage of our products as a result of a failure of our facilities or the facilities or operations of third-party providers to pass any regulatory agency inspection could significantly impair our ability to develop and commercialize our products. This could increase our costs, cause us to lose revenue or market share and damage our reputation.

The FDA and various regulatory agencies outside the U.S. have inspected and approved our commercial manufacturing facilities. We cannot guarantee that the FDA or any other regulatory agencies will approve any other facility we or our third-party providers may operate or, once approved, that any of these facilities will remain in compliance with cGMP and other regulations. Any third party we use to manufacture bulk drug product must be licensed by the FDA and, for controlled substances, the DEA. Failure by us or our third-party providers to gain or maintain regulatory compliance with the FDA or other regulatory agencies could materially adversely affect our business, financial condition, cash flows and results of operations.

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Revenues generated by sales of our products depend on the availability from third-party payers of reimbursement for our products and the extent of cost-sharing arrangements for patients (e.g., patient co-payment, co-insurance, deductible obligations), and any cost-control measures imposed, reductions in payment rate or reimbursement or increases in our financial obligation to payers could result in decreased sales of our products and decreased revenues.

In both U.S. and non-U.S. markets, sales of our products depend, in part, on the availability of reimbursement from third-party payers such as state and federal governments, including Medicare and Medicaid in the U.S. and similar programs in other countries, managed care providers and private insurance plans. Deterioration in the timeliness, certainty and amount of reimbursement for our products, the existence of barriers to coverage of our products (such as prior authorization, criteria for use or other requirements), increases in our financial obligation to payers, including government payers (including due to changes in our AMP calculation), limitations by healthcare providers on how much, or under what circumstances, they will prescribe or administer our products or unwillingness by patients to pay any required co-payments, or deductible amounts, could reduce the use of, and revenues generated from, our products and could have a material adverse effect on our business, financial condition, cash flows and results of operations. In addition, when a new product is approved, the availability of government and private reimbursement for that product is uncertain, as is the amount for which that product will be reimbursed. We cannot predict the availability or amount of reimbursement for our products.

In the U.S., federal and state legislatures, health agencies and third-party payers continue to focus on containing the cost of healthcare, including by comparing the effectiveness, benefits and costs of similar treatments. Any adverse findings for our products from such comparisons may reduce the extent of reimbursement for our products. Economic pressure on state budgets may result in states increasingly seeking to achieve budget savings through mechanisms that limit coverage or payment for drugs, including but not limited to price control initiatives, discounts and other pricing-related actions. For example, in 2017, the State of California enacted as law SB-17, a drug pricing transparency bill that requires, among other things, that manufacturers notify the state and health insurers, and justify, any time such manufacturers plan to increase the price of a medication by sixteen percent (16%) or more over a two-year period. Similar state drug pricing initiatives were enacted in 2018 (e.g., Oregon HB 4005 with reporting requirements commencing in 2019) and we expect additional state drug pricing initiatives to be proposed and enacted in 2019. In addition, State Medicaid programs are increasingly requesting manufacturers to pay supplemental rebates and requiring prior authorization by the state program for use of any drug. Managed care organizations continue to seek price discounts and, in some cases, to impose restrictions on the coverage of particular drugs. Government efforts to reduce Medicaid expenses may lead to increased use of managed care organizations by Medicaid programs. This may result in managed care organizations influencing prescription decisions for a larger segment of the population and a corresponding constraint on prices and reimbursement for our products.

In 2019, we may face uncertainties as a result of likely continued federal and administrative efforts to repeal, substantially modify or invalidate some or all of the provisions of the PPACA and potential reforms and changes to government negotiation or regulation of drug pricing. For example, on January 31, 2019, HHS released a notice of proposed rulemaking as part of ongoing administration drug pricing reform efforts that would modify a regulatory provision that had previously protected certain pharmaceutical manufacturer rebates from criminal prosecution and financial penalties under the federal Anti-Kickback Statute and that would add new regulatory safe harbors for certain price reductions passed through to dispensing pharmacies and payments to pharmacy benefit managers. There is no assurance that such efforts and proposed legislation will not adversely affect our business and financial results, and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform and drug pricing will affect our business.

The government-sponsored healthcare systems in Europe and many other countries are the primary payers for healthcare expenditures, including payment for drugs and biologics. We expect that countries may take actions to reduce expenditure on drugs and biologics, including mandatory price reductions, patient access restrictions,

suspensions of price increases, increased mandatory discounts or rebates, preference for generic products, reduction in the amount of reimbursement and greater importation of drugs from lower-cost countries. These cost-control measures likely would reduce our revenues. In addition, certain countries set prices by reference to the prices in other countries where our products are marketed. Thus, the inability to secure adequate prices in a particular country may not only limit the marketing of products within that country, but may also adversely affect the ability to obtain acceptable prices in other markets.

Patent protection for our products is important and uncertain.

The following factors are important to our success:

- receiving and maintaining patent and/or trademark protection for our products, technologies and developing technologies, including those that are subject to our licensing arrangements;
- maintaining our trade secrets;
- not infringing the proprietary rights of others; and
- preventing others from infringing our proprietary rights.

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Patent protection only provides rights of exclusivity for the term of the patent. We are able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. In this regard, we try to protect our proprietary position by filing patent applications in the U.S. and elsewhere related to our proprietary product inventions and improvements that are important to our business and products. Our pending patent applications, together with those we may file in the future, or those we may license to or from third parties, may not result in patents being issued. Even if issued, such patents may not provide us with sufficient proprietary protection or competitive advantages against competitors with similar technology. The development of new technologies or products may take a number of years, and there can be no assurance that any patents which may be granted in respect of such technologies or products will not have expired or be due to expire by the time such products are commercialized, or that such patents will successfully withstand any challenges during their respective terms.

Although we believe that we make reasonable efforts to protect our intellectual property rights and to ensure that our proprietary technology does not infringe the rights of third parties, we cannot ascertain the existence of all potentially conflicting intellectual property claims. Therefore, there is a risk that third parties may make claims of infringement against our products or technologies. There may be patents issued to, or patent applications filed by, third parties that relate to certain of our products. If patents exist or are issued that cover our products, we may not be able to manufacture, use, offer for sale, sell or import such products without first getting a license from the patent holder. The patent holder may not grant us a license on reasonable terms, or it may refuse to grant us a license at all. This could delay or prevent us from developing, manufacturing, selling or importing those of our products that would require the license. Claims of intellectual property infringement also might require us to redesign affected products, enter into costly settlement or license agreements or pay costly damage awards, or face a temporary or permanent injunction prohibiting us from marketing or selling certain of our products. Even if we have an agreement to indemnify us against such costs, the indemnifying party may be unable to uphold its contractual obligations. If we cannot or do not license the infringed technology at all, license the technology on reasonable terms or substitute similar technology from another source, our business, financial condition, cash flows and results of operations could be materially adversely affected.

Because the patent positions of biopharmaceutical companies involve complex legal and factual questions, enforceability of patents cannot be predicted with certainty. The ultimate degree of patent protection that will be afforded to products and processes, including ours, and those of our licensees, in the U.S. and in other important markets, remains uncertain and is dependent upon the scope of protection decided upon by the patent offices, courts and lawmakers in these countries. Patents, if issued, may be challenged, invalidated or circumvented. As more products are commercialized using our proprietary product platforms, or as any product achieves greater commercial success, our patents become more likely to be subject to challenge by potential competitors. The laws of certain countries may not protect our intellectual property rights to the same extent as do the laws of the U.S., and any patents that we own or license from others may not provide any protection against competitors. Furthermore, others may independently develop similar technologies outside the scope of our patent coverage.

We also rely on trade secrets, know-how and technology, which are not protected by patents, to maintain our competitive position. We try to protect this information by entering into confidentiality agreements with parties that have access to it, such as our licensees, licensors, contract manufacturers, potential business partners, employees and consultants. Any of these parties may breach the agreements and disclose our confidential information, or our competitors might learn of the information in some other way. To the extent that our employees, consultants or contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to, or independently developed by, a competitor, such event could materially adversely affect our business, financial condition, cash flows and results of operations.

Uncertainty over intellectual property in the biopharmaceutical industry has been the source of litigation, which is inherently costly and unpredictable, could significantly delay or prevent approval or commercialization of our products, and could adversely affect our business.

There is considerable uncertainty within the biopharmaceutical industry about the validity, scope and enforceability of many issued patents in the U.S. and elsewhere in the world. We cannot currently determine the ultimate scope and validity of patents which may be granted to third parties in the future or which patents might be asserted to be infringed by the manufacture, use or sale of our products.

In part as a result of this uncertainty, there has been, and we expect that there may continue to be, significant litigation and an increasing number of IPRs and administrative proceedings in the pharmaceutical industry regarding patents and other intellectual property rights. A patent holder might file an IPR, interference and/or infringement action against us, including in response to patent certifications required under the Hatch-Waxman Act, claiming that certain claims of one or more of our issued patents are invalid or that the manufacture, use, offer for sale, sale or import of our products infringed one or more of such party's patents. We may have to expend considerable time, effort and resources to defend such actions. In addition, we may need to enforce our intellectual property rights against third parties who infringe our patents and other intellectual property or challenge our patents, patent applications or trademark applications (see "—We or our licensees may face claims against our intellectual property rights covering our products and competition from generic drug manufacturers" for additional information regarding litigation with generic drug manufacturers). We expect that litigation may be necessary in some instances to determine the validity and scope of certain of our proprietary rights. Competitors may sue us as a way of delaying the introduction of our products.

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Litigation and trial proceedings, such as IPRs, concerning patents and other intellectual property rights may be expensive, protracted with no certainty of success, and distracting to management. Ultimately, the outcome of such litigation and proceedings could adversely affect our business and the validity and scope of our patents or other proprietary rights or delay or prevent us from manufacturing and marketing our products.

We rely on a limited number of pharmaceutical wholesalers to distribute our products.

As is typical in the pharmaceutical industry, we utilize pharmaceutical wholesalers in connection with the distribution of the products that we market and sell. A significant amount of our product is sold to end-users through the three largest wholesalers in the U.S. market, Cardinal Health Inc., AmerisourceBergen Corp. and McKesson Corp. If we are unable to maintain our business relationships with these major pharmaceutical wholesalers on commercially acceptable terms, if the buying patterns of these wholesalers fluctuate due to seasonality or if wholesaler buying decisions or other factors outside of our control change, such events could materially adversely affect our business, financial condition, cash flows and results of operations.

Our business may suffer if we are unable to develop new products.

Our long-term viability and growth will be significantly impacted by our ability to successfully develop new products from our research and development activities and we expect the development of products for our own account to consume substantial resources. Since we fund the development of our proprietary products, there is a risk that we may not be able to continue to fund all such development efforts to completion or to provide the support necessary to perform the clinical trials, obtain regulatory approvals, obtain a final DEA scheduling designation (to the extent our products are controlled substances) or market any approved products on a worldwide basis. If we develop commercial products on our own, the risks associated with such development programs may be greater than those associated with our programs that are developed with licensees.

If our delivery technologies or product development efforts fail to result in the successful development and commercialization of products, if our licensees decide not to pursue development and/or commercialization of our products or if our products do not perform as anticipated, such events could materially adversely affect our business, financial condition, cash flows and results of operations (see “—Our revenues may be lower than expected as a result of failure by the marketplace to accept our products or for other factors” for factors that may affect the market acceptance of our products approved for sale).

The FDA or other regulatory agencies may impose limitations or post-approval requirements on any product approval.

Even if regulatory approval to market a product is granted by the FDA or other regulatory agencies, the approval may impose limitations on the indicated use for which the product may be marketed or additional post-approval requirements, such as a REMS, with which we would need to comply in order to maintain the approval of such product. Our business could be seriously harmed if we do not complete these post-approval requirements and the FDA or other regulatory agencies, as a result, require us to change the label for our products or if such requirements restrict the marketing, sale or use of our products.

Further, if a product for which we obtain regulatory approval is a controlled substance, it will not become commercially available until after the DEA provides its final schedule designation, which may take longer and may be more restrictive than we expect or may change after its initial designation. We currently expect ALKS 3831, if approved, to require such DEA final schedule designation prior to commercialization. A restrictive designation could adversely affect our ability to commercialize such products and could materially adversely affect our business, financial condition, cash flows and results of operations.

In addition, legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the commercialization of our products, if any, may be.

Litigation, arbitration or regulatory action (such as citizens petitions) filed against regulatory agencies related to our product or Alkermes, including securities litigation, may result in financial losses, harm our reputation, divert management resources, negatively impact the approval of our products, or otherwise negatively impact our business.

We may be the subject of certain claims, including those asserting violations of securities and fraud and abuse laws and derivative actions. Following periods of volatility in the market price of a company's securities, securities class action litigation has often been instituted against companies. For example, in November 2017, a purported stockholder of ours filed a putative class action against us and certain of our officers on behalf of a putative class of purchasers of our securities during the period of February 24, 2015 through November 14, 2017. Such action alleges violations of Sections 10(b) and 20(a) of the Exchange Act based on allegedly false or misleading statements and omissions regarding our marketing practices related to VIVITROL, and seeks to recover unspecified damages for alleged inflation in the price of securities, and reasonable costs and expenses, including attorneys' fees. In December 2018 and January 2019, two purported stockholders of ours filed putative class actions against us and certain of our officers on behalf of a putative class of purchasers of our securities during the period of February 17, 2017 through November 1, 2018. Such actions allege violations of Sections 10(b) and 20(a) of the Exchange Act based on allegedly false or misleading statements and

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omissions regarding our regulatory submission for ALKS 5461, our drug candidate for the adjunctive treatment of major depressive disorder, and the FDA's review and consideration of that submission, and seeks to recover unspecified money damages, prejudgment and postjudgment interest, reasonable attorneys' fees, expert fees and other costs. For further discussion of these putative class actions, see Note 16, Commitments and Contingent Liabilities in the "Notes to Consolidated Financial Statements" and "Item 3—Legal Proceedings" in this Annual Report. These class actions and any similar future litigation could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

We may be the subject of certain government inquiries or requests for documentation. For example, in June 2017 we received a subpoena from an Office of the U.S. Attorney, and in January 2019 we received a civil investigative demand from an Office of the U.S. Attorney, in each case for documents related to VIVITROL. We are cooperating with the government. If, as a result of the government's requests, proceedings are initiated and we are found to have violated one or more applicable laws, we may be subject to significant liability, including without limitation, civil fines, criminal fines and penalties, civil damages and exclusion from federal funded healthcare programs such as Medicare and Medicaid, as well as potential liability under the federal anti-kickback statute and False Claims Act and state False Claims Acts, and may be required to enter into a corporate integrity or other settlement with the government, any of which could materially affect our reputation, business, financial condition, cash flows and results of operations. Conduct giving rise to such liability could also form the basis for private civil litigation by third-party payers or other persons allegedly harmed by such conduct. In addition, if some of our existing business practices are challenged as unlawful, we may have to change those practices, including changes and impacts on the practices of our sales force, which could also have a material adverse effect on our business, financial condition, cash flows and results of operations.

We may not be successful in defending ourselves in litigation or arbitration which may result in large judgments or settlements against us, which could have a negative effect on our business, financial condition, cash flows and results of operations. Further, our liability insurance coverage may not be sufficient to satisfy, or may not cover, any expenses or liabilities that may arise. Additionally, regardless of whether or not there is merit to the claims underlying any lawsuits or government inquiries of which we are subject, or whether or not we are found as a result of such lawsuits or inquiries to have violated any applicable laws, such lawsuits and inquiries can be expensive to defend or respond to, may divert the attention of our management and other resources that would otherwise be engaged in managing our business, and may further cause significant and potentially irreparable harm to our public reputation.

We may also be the subject of citizen petitions that request that the FDA refuse to approve, delay approval of, or impose additional approval requirements for our NDAs. If successful, such petitions can significantly delay, or even prevent, the approval of the NDA in question. Even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition or impose additional approval requirements as a result of such petition. These outcomes and others could adversely affect our share price as well as our ability to generate revenues from the commercialization and sale of our products and products using our proprietary technologies.

If we fail to comply with the extensive legal and regulatory requirements affecting the healthcare industry, we could face costs, penalties and a loss of business.

Our activities, and the activities of our licensees and third-party providers, are subject to extensive government regulation. Government regulation by various national, state and local agencies, which includes detailed inspection of, and controls over, research and laboratory procedures, clinical investigations, product approvals and manufacturing, marketing and promotion, adverse event reporting, sampling, distribution, recordkeeping, storage, and disposal practices, and achieving compliance with these regulations, substantially increases the time, difficulty and costs incurred in obtaining and maintaining approvals to market newly developed and existing products. Government

regulatory actions can result in delay in the release of products, seizure or recall of products, suspension or revocation of the authority necessary for the manufacture and sale of products, and other civil or criminal sanctions, including fines and penalties. Biopharmaceutical companies also have been the target of government lawsuits and investigations alleging violations of government regulation, including claims asserting submission of incorrect pricing information, impermissible off-label promotion of pharmaceutical products, payments intended to influence the referral of healthcare business, submission of false claims for government reimbursement, antitrust violations and violations related to environmental matters. In addition, we may be the subject of securities law claims and derivative actions.

While we have implemented numerous risk mitigation measures, we cannot guarantee that we, our employees, our licensees, our consultants or our contractors are, or will be, in compliance with all applicable U.S. federal and state laws and regulations, applicable laws and regulations outside the U.S., and interpretations of the applicability of these laws to marketing practices. If we or our agents fail to comply with any of those regulations or laws, a range of actions could result, including the termination of clinical trials, the failure to approve a product, restrictions on our products or manufacturing processes, withdrawal of our products from the market, significant fines, exclusion from government healthcare programs or other sanctions or litigation.

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Changes affecting the healthcare industry, including new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to patent protection and enforcement, healthcare availability, and product pricing and marketing, could also adversely affect our revenues and our potential to be profitable. For example, the costs of prescription pharmaceuticals in the U.S. has been the subject of considerable discussion in the U.S. and the current administration has stated that it will address such costs through new legislative and administrative measures. On January 31, 2019, HHS released a notice of proposed rulemaking as part of ongoing administration drug pricing reform efforts that would modify a regulatory provision that had previously protected certain pharmaceutical manufacturer rebates from criminal prosecution and financial penalties under the federal Anti-Kickback Statute and that would add new regulatory safe harbors for certain price reductions passed through to dispensing pharmacies and payments to pharmacy benefit managers. Such changes in law, regulation and the interpretation of existing laws and regulations could have a material adverse effect on our business, financial condition, cash flows and results of operations.

We face competition in the biopharmaceutical industry.

We face intense competition in the development, manufacture, marketing and commercialization of our products from many and varied sources, such as research institutions and biopharmaceutical companies, including other companies with similar technologies, and manufacturers of generic drugs (see "—We or our licensees may face claims against our intellectual property rights covering our products and competition from generic drug manufacturers." for additional information relating to competition from generic drug manufacturers). Some of these competitors are also our licensees, who control the commercialization of products from which we receive manufacturing and/or royalty revenues. These competitors are working to develop and market other systems, products, and other methods of preventing or reducing disease, and new small-molecule and other classes of drugs that can be used with or without a drug delivery system.

The biopharmaceutical industry is characterized by intensive research, development and commercialization efforts and rapid and significant technological change. Many of our competitors are larger and have significantly greater financial and other resources than we do. We expect our competitors to attempt to develop new technologies, products and processes that may be more effective than those we develop. The development of technologically improved or different products or technologies may make our products or product platforms obsolete or noncompetitive before we recover expenses incurred in connection with their development or realize any revenues from any product.

There are other companies developing extended-release product platforms. In many cases, there are products on the market or in development that may be in direct competition with our products. In addition, we know of new chemical entities that are being developed that, if successful, could compete against our products. These chemical entities are being designed to work differently than our products and may turn out to be safer or more effective than our products. Among the many experimental therapies being tested around the world, there may be some that we do not now know of that may compete with our proprietary product platforms or products. Our licensees could choose a competing technology to use with their drugs instead of one of our product platforms and could develop products that compete with our products.

With respect to our proprietary injectable product platform, we are aware that there are other companies developing extended-release delivery systems for pharmaceutical products, including, but not limited to Luye Pharma, which is developing risperidone formulated as extended release microspheres for intramuscular injection for the treatment of schizophrenia and/or schizoaffective disorders. In the treatment of schizophrenia, ARISTADA, INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA and RISPERDAL CONSTA compete with each other and a number of other injectable products including ZYPREXA RELPREVV ((olanzapine) For Extended Release Injectable Suspension), which is marketed and sold by Lilly; ABILIFY MAINTENA, (aripiprazole for extended release injectable suspension), a once-monthly injectable formulation of ABILIFY (aripiprazole) developed by Otsuka

Pharm. Co.; PERSERIS (risperidone for extended release injectable suspension), a once-monthly formulation of risperidone marketed by Indivior plc; oral compounds currently on the market; and generic versions of branded oral and injectable products. In the treatment of bipolar disorder, RISPERDAL CONSTA competes with antipsychotics such as oral aripiprazole, REXULTI, LATUDA, VRYLAR, ABILIFY MAINTENA, risperidone, quetiapine, olanzapine, ziprasidone and clozapine.

In the treatment of alcohol dependence, VIVITROL competes with generic acamprosate calcium (also known as CAMPRAL) and generic disulfiram (also known as ANTABUSE) as well as currently marketed drugs, including generic drugs, also formulated from naltrexone. Other pharmaceutical companies are developing products that have shown some promise in treating alcohol dependence that, if approved by the FDA, would compete with VIVITROL.

In the treatment of opioid dependence, VIVITROL competes with SUBOXONE (buprenorphine HCl/naloxone HCl dehydrate sublingual tablets), SUBOXONE (buprenorphine/naloxone) Sublingual Film, SUBUTEX (buprenorphine HCl sublingual tablets) and SUBLOCADE (once-monthly buprenorphine extended-release injection), each of which is marketed and sold by Indivior plc, and BUNAVAIL buccal film (buprenorphine and naloxone) marketed by BioDelivery Sciences, PROBUPHINE (buprenorphine) from Titan Pharmaceuticals, Inc. and ZUBSOLV (buprenorphine and naloxone) marketed by Orexo US, Inc., and once launched, will compete with BRIXADI, which will be marketed by Braeburn, Inc. It also competes with methadone, oral naltrexone and generic versions of SUBUTEX and SUBOXONE sublingual tablets. Other pharmaceutical companies are developing products that have shown promise in treating opioid dependence that, if approved by the FDA, would compete with VIVITROL.

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While AMPYRA/FAMPYRA is approved as a treatment to improve walking in patients with MS, there are a number of FDA-approved therapies for MS disease management that seek to reduce the frequency and severity of exacerbations or slow the accumulation of physical disability for people with certain types of MS. These products include AVONEX, TYSABRI, TECFIDERA, and PLEGRIDY from Biogen; OCREVUS from Genentech; BETASERON from Bayer HealthCare Pharmaceuticals; COPAXONE from Teva Pharmaceutical Industries Ltd.; REBIF and NOVANTRONE from EMD Serono, Inc.; GILENYA and EXTAVIA from Novartis AG; AUBAGIO and LEMTRADA from Sanofi-Aventis, and generic products, including generic versions of AMPYRA.

With respect to our NanoCrystal technology, we are aware that other technology approaches similarly address poorly water-soluble drugs. These approaches include nanoparticles, cyclodextrins, lipid-based self-emulsifying drug delivery systems, dendrimers and micelles, among others, any of which could limit the potential success and growth prospects of products incorporating our NanoCrystal technology. In addition, there are many competing technologies to our OCR technology, some of which are owned by large pharmaceutical companies with drug delivery divisions and other, smaller drug delivery-specific companies.

If we are unable to compete successfully in the biopharmaceutical industry, our business, financial condition, cash flows and results of operations could be materially adversely affected.

We or our licensees may face claims against intellectual property rights covering our products and competition from generic drug manufacturers.

In the U.S., generic manufacturers of innovator drug products may file ANDAs and, in connection with such filings, certify that their products do not infringe the innovator's patents and/or that the innovator's patents are invalid. This often results in litigation between the innovator and the ANDA applicant. This type of litigation is commonly known in the U.S. as "Paragraph IV" litigation.

For example, we and our partner Acorda received notices of numerous ANDA filings challenging the validity of one or more of the Orange Book-listed patents for AMPYRA and/or asserting that a generic form of AMPYRA would not infringe such patents, and we and Acorda engaged in Paragraph IV litigation with various ANDA filers disputing such claims. For further discussion of the legal proceedings related to the patents covering AMPYRA, see Note 16, Commitments and Contingent Liabilities in the "Notes to Consolidated Financial Statements" and "Item 3—Legal Proceedings" in this Annual Report.

Similarly, Janssen Pharmaceuticals NV and Janssen Pharmaceuticals, Inc. initiated a patent infringement lawsuit against Teva Pharmaceuticals USA, Inc. ("Teva"), who filed an ANDA seeking approval to market a generic version of INVEGA SUSTENNA. For a discussion of the legal proceedings related to the patents covering INVEGA SUSTENNA, see Note 16, Commitments and Contingent Liabilities in the "Notes to Consolidated Financial Statements" and "Item 3—Legal Proceedings" in this Annual Report.

Although we intend to vigorously enforce our intellectual property rights, and we expect our licensees will do the same, there can be no assurance that we or our licensees will prevail in defense of such patent rights. Our and our licensees' existing patents could be invalidated, found unenforceable or found not to cover generic forms of our or our licensees' products. If an ANDA filer were to receive FDA approval to sell a generic version of our products and/or prevail in any patent litigation, our products would become subject to increased competition and our business, financial condition, cash flows and results of operations could be materially adversely affected.

The commercial use of our products may cause unintended side effects or adverse reactions, or incidents of misuse may occur, which could adversely affect our business and share price.

We cannot predict whether the commercial use of our products will produce undesirable or unintended side effects that have not been evident in the use of, or in clinical trials conducted for, such products to date. The administration of drugs in humans carries the inherent risk of product liability claims whether or not the drugs are actually the cause of an injury. Our products may cause, or may appear to have caused, injury or dangerous drug interactions, and we may not learn about or understand those effects until the products have been administered to patients for a prolonged period of time. Additionally, incidents of product misuse may occur.

These events, among others, could result in product recalls, product liability actions or withdrawals or additional regulatory controls (including additional regulatory scrutiny, REMS programs, and requirements for additional labeling). As our development activities progress and we continue to have commercial sales, this product liability insurance coverage may be inadequate to satisfy liabilities that arise, we may be unable to obtain adequate coverage at an acceptable cost or at all, or our insurer may disclaim coverage as to a future claim. This could prevent or limit our commercialization of our products. In addition, the reporting of adverse safety events involving our products, including instances of product misuse, and public rumors about such events could cause our product sales or share price to decline or experience periods of volatility. These types of events could have a material adverse effect on our business, financial condition, cash flows and results of operations.

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Our business involves environmental, health and safety risks.

Our business involves the use of hazardous materials and chemicals and is subject to numerous environmental, health and safety laws and regulations and to periodic inspections for possible violations of these laws and regulations. Under certain of these laws and regulations, we could be liable for any contamination at our current or former properties or third-party waste disposal sites. In addition to significant remediation costs, contamination can give rise to third-party claims for fines, penalties, natural resource damages, personal injury and damage (including property damage). The costs of compliance with environmental, health and safety laws and regulations are significant. Any violations, even if inadvertent or accidental, of current or future environmental, health or safety laws or regulations, or the cost of compliance with any resulting order or fine and any liability imposed in connection with any contamination for which we may be responsible, could materially adversely affect our business, financial condition, cash flows and results of operations.

We may not become profitable on a sustained basis.

At December 31, 2018, our accumulated deficit was $1,185.4 million, which was primarily the result of net losses incurred from 1987, the year Alkermes, Inc., was founded, through December 31, 2018, partially offset by net income over certain fiscal periods. There can be no assurance we will achieve sustained profitability.

A major component of our revenue is dependent on our and our licensees' ability to commercialize our products and to manufacture our products economically. Our ability to achieve sustained profitability in the future depends, in part, on our or our licensees' (as applicable) ability to:

- successfully commercialize VIVITROL, ARISTADA and ARISTADA INITIO and any other products that may be marketed in the U.S. or in other countries in which such products are approved;
- obtain and maintain regulatory approval for products both in the U.S. and in other countries;
- efficiently manufacture our products;
- support the commercialization of products by our licensees;
- enter into agreements to develop and commercialize our products;
- develop, have manufactured or expand our capacity to manufacture successfully and cost effectively, and market, our products;
- obtain adequate reimbursement coverage for our products from insurance companies, government programs and other third-party payers;
- obtain additional research and development funding for our proprietary products; and
- achieve certain product development milestones.

In addition, the amounts we spend will impact our profitability. Our spending will depend, in part, on:

- the progress of our research and development programs for our products, including pre-clinical and clinical trials;
- the time and expense that will be required to pursue FDA and/or other regulatory approvals for our products and whether such approvals are obtained;
- the time that will be required for the DEA to provide its final scheduling designation for our approved products that are controlled substances;
- the time and expense required to prosecute, enforce, defend and/or challenge patent and other intellectual property rights;
- the cost of building, operating and maintaining manufacturing and research facilities;
- the cost of third-party manufacturers;
- the number of products we pursue, particularly proprietary products;
- how competing technological and market developments affect our products;
- the cost of possible acquisitions of technologies, compounds, product rights or companies;

- the cost of obtaining licenses to use technology or intellectual property rights owned by others for proprietary products and otherwise;

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- the costs related to potential litigation, arbitration or government requests for information; and
- the costs associated with recruiting, compensating and retaining a highly skilled workforce in an environment where competition for such employees is intense.

We may not achieve all or any of these goals, and thus we cannot provide assurances that we will ever be profitable on a sustained basis or achieve significant revenues. Even if we do achieve some or all of these goals, we may not achieve significant or sustained commercial success.

Our level of indebtedness could adversely affect our business and limit our ability to plan for or respond to changes in our business.

In March 2018, we amended and refinanced the term loan under our credit agreement, (previously referred to as "Term Loan B-1", and as so amended and refinanced, the "2023 Term Loans"), in order to, among other things, extend the due date of the loan from September 25, 2021 to March 26, 2023, reduce the interest payable thereon from LIBOR plus 2.75% with a LIBOR floor of 0.75% to LIBOR plus 2.25% with a 0% LIBOR floor and increase covenant flexibility. As of December 31, 2018, our borrowings consisted of $282.1 million outstanding under the 2023 Term Loans.

The 2023 Term Loans are secured by a first priority lien on substantially all of the combined company assets and properties of Alkermes plc and most of its subsidiaries, which serve as guarantors. The agreements governing the 2023 Term Loans include a number of restrictive covenants that, among other things, and subject to certain exceptions and baskets, impose operating and financial restrictions on us. Our level of indebtedness and the terms of these financing arrangements could adversely affect our business by, among other things:

- requiring us to dedicate a substantial portion of our cash flow from operations to payments on our indebtedness, thereby reducing the availability of our cash flow for other purposes, including business development efforts, research and development, commercial and capital expenditures;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate, thereby placing us at a competitive disadvantage compared to competitors with less debt;
- limiting our ability to take advantage of significant business opportunities, such as potential acquisition opportunities; and
- increasing our vulnerability to adverse economic and industry conditions.

Our failure to comply with these restrictions or to make these payments could lead to an event of default that could result in an acceleration of the indebtedness. Our future operating results may not be sufficient to ensure compliance with these covenants or to remedy any such default. In the event of an acceleration of this indebtedness, we may not have, or be able to obtain, sufficient funds to make any accelerated payments.

Discontinuation, reform or replacement of LIBOR, or uncertainty related to the potential for any of the foregoing, may adversely affect us.

In July 2017, the U.K. Financial Conduct Authority announced that LIBOR could be effectively discontinued after 2021. In addition, other regulators have suggested reforming or replacing other benchmark rates. The discontinuation, reform or replacement of LIBOR or any other benchmark rates may have an unpredictable impact on contractual mechanics in the credit markets or cause disruption to the broader financial markets. Uncertainty as to the nature of such potential discontinuation, reform or replacement may negatively impact the volatility of LIBOR rates, liquidity, our access to funding required to operate our business, or the trading market for our 2023 Term Loans.

Under our 2023 Term Loans, if the administrative agent determines that LIBOR is not reasonably ascertainable, or is notified by our lenders that LIBOR does not adequately and fairly reflect the costs to our lenders of maintaining the loans, we would be required to pay interest under an alternative base rate which could cause the amount of interest payable on the 2023 Term Loans to be materially different than expected. We may choose in the future to pursue an

amendment to our 2023 Term Loans to provide for a transition mechanism or other alternative reference rate in anticipation of LIBOR's discontinuation, but we can give no assurance that we will be able to reach agreement with our lenders on any such amendment.

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We may require additional funds to execute on our business strategy, and such funding may not be available on commercially favorable terms or at all and may cause dilution to our existing shareholders.

We may require additional funds in the future to execute on our business strategy, and we may seek funds through various sources, including debt and equity offerings, corporate collaborations, bank borrowings, arrangements relating to assets, sale of royalty streams we receive on our products or other financing methods or structures. The source, timing and availability of any financings will depend on market conditions, interest rates and other factors. If we issue additional equity securities or securities convertible into equity securities to raise funds, our shareholders will suffer dilution of their investment, and it may adversely affect the market price of our ordinary shares. In addition, as a condition to providing additional funds to us, future investors or lenders may demand, and may be granted, rights superior to those of existing shareholders. If we issue additional debt securities in the future, our existing debt service obligations will increase further. If we are unable to generate sufficient cash to meet these obligations and need to use existing cash or liquidate investments in order to fund our debt service obligations or to repay our debt, we may be forced to delay or terminate clinical trials or curtail operations. We cannot be certain, however, that additional financing will be available from any of these sources when needed or, if available, will be on acceptable terms, if at all, particularly if the credit and financial markets are constrained at the time we require funding. If we fail to obtain additional capital when we need it, we may not be able to execute our business strategy successfully and may have to give up rights to our product platforms, and/or products, or grant licenses on terms that may not be favorable to us.

Adverse financial market conditions may exacerbate certain risks affecting our business.

As a result of adverse financial market conditions, organizations that reimburse for use of our products, such as government health administration authorities and private health insurers, may be unable to satisfy such obligations or may delay payment. In addition, federal and state health authorities may reduce reimbursements (including Medicare and Medicaid reimbursements in the U.S.) or payments, and private insurers may increase their scrutiny of claims. We are also dependent on the performance of our licensees, and we sell our products to our licensees through contracts that may not be secured by collateral or other security. Accordingly, we bear the risk if our licensees are unable to pay amounts due to us thereunder. Due to volatility in the financial markets, there may be a disruption or delay in the performance of our third-party contractors, suppliers or licensees. If such third parties are unable to pay amounts owed to us or satisfy their commitments to us, or if there are reductions in the availability or extent of reimbursement available to us, our business, financial condition, cash flows and results of operations would be adversely affected.

Currency exchange rates may affect revenues and expenses.

We conduct a large portion of our business in international markets. For example, we derive a majority of our RISPERDAL CONSTA revenues and all of our FAMPYRA, XEPLION and TREVICTA revenues from sales in countries other than the U.S., and these sales are denominated in non-U.S. dollar (“USD”) currencies. We also incur substantial operating costs in Ireland and face exposure to changes in the exchange ratio of the USD and the Euro arising from expenses and payables at our Irish operations that are settled in Euro. Our efforts to mitigate the impact of fluctuating currency exchange rates may not be successful. As a result, currency fluctuations among our reporting currency, USD, and the currencies in which we do business will affect our results of operations, often in unpredictable ways. Refer to “Item 7A—Quantitative and Qualitative Disclosures about Market Risk” for additional information relating to our foreign currency exchange rate risk.

Our future success largely depends upon our ability to attract and retain key personnel.

Our ability to compete and succeed in the highly competitive biopharmaceutical industry and in the disease states in which we market and sell products depends largely upon the continued service of our management and scientific and commercial teams and our ability to attract, retain and motivate highly skilled technical, scientific, manufacturing,

management, regulatory, compliance and selling and marketing personnel. Each of our executive officers and all of our employees are employed "at will," meaning we or each officer or employee may terminate the employment relationship at any time. The loss of key personnel or our inability to hire and retain personnel who have technical, scientific, manufacturing, management, regulatory, compliance or commercial backgrounds could materially adversely impact our business, including the achievement of our manufacturing, research and development, commercial and other business objectives.

Future transactions may harm our business or the market price of our ordinary shares.

We regularly review potential transactions related to technologies, products or product rights and businesses complementary to our business. These transactions could include:

- mergers;
- acquisitions;
- strategic alliances;

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- licensing agreements; and
- co-promotion agreements.

We may choose to enter into one or more of these transactions at any time, which may cause substantial fluctuations in the market price of our ordinary shares. Moreover, depending upon the nature of any transaction, we may experience a charge to earnings, which could also materially adversely affect our results of operations and could harm the market price of our ordinary shares.

If we are unable to successfully integrate the companies, businesses or assets that we acquire, or we are unable to integrate successfully with a company who acquires our company, business or assets, such events could materially adversely affect our business, financial condition, cash flows and results of operations.

Mergers, acquisitions and other strategic transactions involve various inherent risks, including:

- uncertainties in assessing the value, strengths and potential profitability of, and identifying the extent of all weaknesses, risks, contingent and other liabilities of, the respective parties;
- the potential loss of key customers, management and employees of an acquired business;
- the consummation of financing transactions, acquisitions or dispositions and the related effects on our business;
- the ability to achieve identified operating and financial synergies from an acquisition in the amounts and within the timeframe predicted;
- problems that could arise from the integration of the respective businesses, including the application of internal control processes to the acquired business;
- difficulties that could be encountered in managing international operations; and
- unanticipated changes in business, industry, market or general economic conditions that differ from the assumptions underlying our rationale for pursuing the transaction.

Any one or more of these factors could cause us not to realize the benefits anticipated from a transaction. Moreover, any acquisition opportunities we pursue could materially affect our liquidity and capital resources and may require us to incur additional indebtedness, seek equity capital or both, which could result in significant dilution to our shareholders. Future acquisitions could also result in our assuming more long-term liabilities relative to the value of the acquired assets than we have assumed in our previous acquisitions.

If goodwill or other intangible assets become impaired, we could have to take significant charges against earnings.

At December 31, 2018, we had $191.0 million of amortizable intangible assets and $92.9 million of goodwill. Under accounting principles generally accepted in the U.S. (“GAAP”), we must assess, at least annually and potentially more frequently, whether the value of goodwill and other indefinite lived intangible assets have been impaired. Amortizing intangible assets will be assessed for impairment in the event of an impairment indicator. Any reduction or impairment of the value of goodwill or other intangible assets will result in a charge against earnings, which could materially adversely affect our results of operations and shareholders’ equity in future periods.

Our effective tax rate may increase.

As a global biopharmaceutical company, we are subject to taxation in a number of different jurisdictions. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of these places. Our effective tax rate may fluctuate depending on a number of factors, including, but not limited to, the distribution of our profits or losses between the jurisdictions where we operate and differences in interpretation of tax laws. In addition, the tax laws of any jurisdiction in which we operate may change in the future, which could impact our effective tax rate. Tax authorities in the jurisdictions in which we operate may audit us. If we are unsuccessful in

defending any tax positions adopted in our submitted tax returns, we may be required to pay taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, any of which could have a material adverse effect on our business, financial condition, cash flows and results of operations.

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Our deferred tax assets may not be realized.

As of December 31, 2018, we had $85.8 million in net deferred tax assets in the U.S. Included in this amount was approximately $38.7 million of research and development tax credit carryforwards that can be used to offset federal tax in future periods. These carryforwards will expire within the next twenty years. It is possible that some or all of the deferred tax assets will not be realized, especially if we incur losses in the U.S. in the future. Losses may arise from unforeseen operating events (see "—We may not become profitable on a sustained basis" for additional information relating to operating losses) or the occurrence of significant excess tax benefits arising from the exercise of stock options and/or the vesting of restricted stock units. Unless we are able to generate sufficient taxable income in the future, a substantial valuation allowance to reduce the carrying value of our U.S. deferred tax assets may be required, which would materially increase our expenses in the period the allowance is recognized and materially adversely affect our business, financial condition and results of operations.

The business combination of Alkermes, Inc. and the drug technology business ("EDT") of Elan Corporation, plc may limit our ability to use our tax attributes to offset taxable income, if any, generated from such business combination.

On September 16, 2011, the businesses of Alkermes, Inc. and EDT were combined under Alkermes plc (this combination is referred to as the "Business Combination"). For U.S. federal income tax purposes, a corporation is generally considered tax resident in the place of its incorporation. Because we are incorporated in Ireland, we should be deemed an Irish corporation under these general rules. However, Section 7874 of the Internal Revenue Code of 1986, as amended (the "Code") generally provides that a corporation organized outside the U.S. that acquires substantially all of the assets of a corporation organized in the U.S. will be treated as a U.S. corporation (and, therefore, a U.S. tax resident) for U.S. federal income tax purposes if shareholders of the acquired U.S. corporation own at least 80% (of either the voting power or the value) of the stock of the acquiring foreign corporation after the acquisition by reason of holding stock in the domestic corporation, and the "expanded affiliated group" (as defined in Section 7874) that includes the acquiring corporation does not have substantial business activities in the country in which it is organized.

In addition, Section 7874 provides that if a corporation organized outside the U.S. acquires substantially all of the assets of a corporation organized in the U.S., the taxable income of the U.S. corporation during the period beginning on the date the first assets are acquired as part of the acquisition, through the date which is ten years after the last date assets are acquired as part of the acquisition, shall be no less than the income or gain recognized by reason of the transfer during such period or by reason of a license of property by the expatriated entity after such acquisition to a foreign affiliate during such period, which is referred to as the "inversion gain," if shareholders of the acquired U.S. corporation own at least 60% (of either the voting power or the value) of the stock of the acquiring foreign corporation after the acquisition by reason of holding stock in the domestic corporation, and the "expanded affiliated group" of the acquiring corporation does not have substantial business activities in the country in which it is organized. If this rule was to apply to the Business Combination, among other things, Alkermes, Inc. would have been restricted in its ability to use the approximately $274.0 million of U.S. federal net operating loss ("NOL") carryforwards and $38.0 million of U.S. state NOL carryforwards that it had as of March 31, 2011. We do not believe that either of these limitations should apply as a result of the Business Combination. However, the U.S. Internal Revenue Service (the "IRS") could assert a contrary position, in which case we could become involved in tax controversy with the IRS regarding possible additional U.S. tax liability. If we were to be unsuccessful in resolving any such tax controversy in our favor, we could be liable for significantly greater U.S. federal and state income tax than we anticipate being liable for through the Business Combination, which would place further demands on our cash needs.

Certain U.S. holders of our ordinary shares may suffer adverse tax consequences if any of our non-U.S. subsidiaries are characterized as a "controlled foreign corporation".

In December 2017, the Tax Cuts and Jobs Act was signed into law. This legislation significantly changes U.S. tax law by, among other things, changing the rules which determine whether a foreign corporation is treated for U.S. tax purposes as a controlled foreign corporation, or CFC, for taxable years ended December 31, 2017 and onwards. The impact of this change on certain holders of our ordinary shares is uncertain and could be adverse, including potential income inclusions and reporting requirements for U.S. persons (as defined in the Internal Revenue Code) who are treated as owning (directly or indirectly) at least 10% of the value or voting power of our shares. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain. Recent changes to these attribution rules relating to the determination of CFC status make it possible that one or more of our non-U.S. subsidiaries will be classified as a CFC. Existing and prospective investors should consult their tax advisers regarding the potential application of these rules to their investments in us.

See “Certain Irish and United States Federal Income Tax Considerations – United States Federal Income Tax Considerations” in our Form S-1/A, filed with the SEC on February 29, 2012, for additional discussion with respect to other potential U.S. federal income tax consequences of investments in us.

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

Proxy contests and other actions by activist shareholders have been waged against many companies in the biopharmaceutical industry over the last few years. If faced with a proxy contest or other activist shareholder action, we may not be able to respond successfully to the contest or action, which could be disruptive to our business. Even if we are successful, our business could be adversely affected by any proxy contest or activist shareholder action involving us because:

- responding to proxy contests and other actions by activist shareholders can be costly and time-consuming, disrupting operations and diverting the attention of management and employees, and can lead to uncertainty;
- perceived uncertainties as to future direction may result in the loss of 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, it may adversely affect our ability to effectively implement our strategic plan in a timely manner and create additional value for our shareholders.

These actions could cause the market price of our ordinary shares to experience periods of volatility.

If any of our licensees undergoes a change in control or in management, this may adversely affect revenues from our products.

Any change of control, or change in management, of our licensees may result in a reprioritization of our product within such licensee's portfolio, or such licensee may fail to maintain the financial or other resources necessary to continue the development and/or commercialization of such product.

If any of our licensees undergoes a change of control and the acquirer either is unable to perform such licensee's obligations under its agreements with us or has a product that competes with ours that such acquirer does not divest, it could materially adversely affect our business, financial condition, cash flows and results of operations.

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

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers and partners, as well as personally identifiable information of patients, clinical trial participants and employees. Similarly, our partners and third-party providers possess certain of our sensitive data. The secure maintenance of this information is critical to our operations and business strategy. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. Certain types of information technology or infrastructure attacks or breaches may go undetected for a prolonged period of time. Any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information, including our data being breached at our partners or third-party providers, could result in legal claims or proceedings and liability under laws that protect the privacy of personal information, disrupt our operations, and damage our reputation which could adversely affect our business.

We may be subject to numerous and varying privacy and security laws, and our failure to comply could result in penalties and reputational damage.

We are subject to laws and regulations covering data privacy and the protection of personal information, including health information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues which may affect our business. In the U.S.,

numerous federal and state laws and regulations, including state security breach notification laws, state health information privacy laws, and federal and state consumer protection laws, govern the collection, use, disclosure, and protection of personal information. Each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues for us. If we fail to comply with applicable laws and regulations we could be subject to penalties or sanctions, including criminal penalties if we knowingly obtain or disclose individually identifiable health information from a covered entity in a manner that is not authorized or permitted by the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA.

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Numerous other countries have, or are developing, laws governing the collection, use and transmission of personal information as well. The EU and other jurisdictions have adopted data protection laws and regulations, which impose significant compliance obligations. In the EU, for example, effective May 25, 2018, the GDPR replaced the prior EU Data Protection Directive (95/46) that governed the processing of personal data in the European Union. The GDPR imposes significant obligations on controllers and processors of personal data, including, as compared to the prior directive, higher standards for obtaining consent from individuals to process their personal data, more robust notification requirements to individuals about the processing of their personal data, a strengthened individual data rights regime, mandatory data breach notifications, limitations on the retention of personal data and increased requirements pertaining to health data, and strict rules and restrictions on the transfer of personal data outside of the EU, including to the U.S. The GDPR also imposes additional obligations on, and required contractual provisions to be included in, contracts between companies subject to the GDPR and their third-party processors that relate to the processing of personal data. The GDPR allows EU member states to make additional laws and regulations further limiting the processing of genetic, biometric or health data.

Adoption of the GDPR increased our responsibility and liability in relation to personal data that we process and may require us to put in place additional mechanisms to ensure compliance. Any failure to comply with the requirements of GDPR and applicable national data protection laws of EU member states, could lead to regulatory enforcement actions and significant administrative and/or financial penalties against us (fines of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher), and could adversely affect our business, financial condition, cash flows and results of operations.

If we identify a material weakness in our internal control over financial reporting, our ability to meet our reporting obligations and the trading price of our ordinary shares could be negatively affected.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected on a timely basis. Accordingly, a material weakness increases the risk that the financial information we report contains material errors.

We regularly review and update our internal controls, disclosure controls and procedures, and corporate governance policies. In addition, we are required under the Sarbanes-Oxley Act of 2002 to report annually on our internal control over financial reporting. Any system of internal controls, however well designed and operated, is based in part on certain assumptions and can provide only reasonable, not absolute, assurances that the objectives of the system are met. If we, or our independent registered public accounting firm, determine that our internal controls over financial reporting are not effective, or we discover areas that need improvement in the future, these shortcomings could have an adverse effect on our business and financial results, and the price of our ordinary shares could be negatively affected.

If we cannot conclude that we have effective internal control over our financial reporting, or if our independent registered public accounting firm is unable to provide an unqualified opinion regarding the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our financial statements, which could lead to a decline in the trading price of our ordinary shares. Failure to comply with reporting requirements could also subject us to sanctions and/or investigations by the SEC, the Nasdaq or other regulatory authorities.

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Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We lease approximately 14,600 square feet of corporate office space in Dublin, Ireland, which houses our corporate headquarters. This lease expires in 2022. We lease two properties in Waltham, Massachusetts. One facility has approximately 175,000 square feet of space and houses corporate offices, administrative areas and laboratories. This lease expires in 2021 and includes a tenant option to extend the term for up to two five-year periods. The second property we lease in Waltham, Massachusetts has approximately 67,000 square feet of office space. This lease expires in 2020 and includes a tenant option to extend the term for up to two one-year periods. We lease approximately 7,000 square feet of corporate office and administrative space in Washington, DC. This lease expires in 2029 and includes a tenant option to extend the term for an additional five-year period.

In March 2018, we entered into a lease agreement for approximately 220,000 square feet of office and laboratory space located in a building to be built at 900 Winter Street, Waltham, Massachusetts ("900 Winter Street"). We plan to occupy the premises in early 2020. The initial term of the lease shall commence on the earlier of (i) the Delivery Date (defined as (i) the later of January 20, 2020, or (ii) the date on which the landlord substantially completes its work in accordance with the terms of the lease), or (ii) the date we enter into possession of all or any substantial portion of 900 Winter Street for the conduct of our business (the "Commencement Date"). The initial lease term expires on the last day of the calendar month in which the fifteenth (15^{th}) anniversary of the Commencement Date occurs, with an option to extend for an additional ten (10) years.

We own an R&D and manufacturing facility in Athlone, Ireland (approximately 400,000 square feet) and a manufacturing facility in Wilmington, Ohio (approximately 360,600 square feet).

We believe that our current and planned facilities are suitable and adequate for our current and near term pre-clinical, clinical and commercial requirements.

Item 3. Legal Proceedings

For information regarding legal proceedings, refer to Note 16, Commitments and Contingent Liabilities in the "Notes to Consolidated Financial Statements" in this Annual Report, which is incorporated into this Part I, Item 3 by reference.

Item 4. Mine Safety Disclosures

Not Applicable.

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PART II

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

Market and shareholder information

Our ordinary shares are traded on the Nasdaq under the symbol "ALKS." There were 119 shareholders of record for our ordinary shares on February 4, 2019. In addition, the last reported sale price of our ordinary shares as reported on the Nasdaq on February 4, 2019 was $33.18.

Dividends

No dividends have been paid on our ordinary shares to date, and we do not expect to pay cash dividends thereon in the foreseeable future. We anticipate that we will retain all earnings, if any, to support our operations and our proprietary drug development programs. Any future determination as to the payment of dividends will be at the sole discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements and other factors our board of directors deems relevant.

Repurchase of equity securities

On September 16, 2011, our board of directors authorized the continuation of the Alkermes, Inc. program to repurchase up to $215.0 million of our ordinary shares at the discretion of management from time to time in the open market or through privately negotiated transactions. We did not purchase any shares under this program during the year ended December 31, 2018. As of December 31, 2018, we had purchased a total of 8,866,342 shares at a cost of $114.0 million. The 2023 Term Loans include restrictive covenants that impose certain limitations on our ability to repurchase our ordinary shares.

During the three months ended December 31, 2018, we acquired 112,733 Alkermes ordinary shares, at an average price of $34.03 per share related to the vesting of employee equity awards to satisfy withholding tax obligations.

Irish taxes applicable to U.S. holders

The following is a general summary of the main Irish tax considerations applicable to the purchase, ownership and disposition of our ordinary shares by U.S. holders. It is based on existing Irish law and practices in effect on January 15, 2019, and on discussions and correspondence with the Irish Revenue Commissioners. Legislative, administrative or judicial changes may modify the tax consequences described below.

The statements do not constitute tax advice and are intended only as a general guide. Furthermore, this information applies only to ordinary shares held as capital assets and does not apply to all categories of shareholders, such as dealers in securities, trustees, insurance companies, collective investment schemes and shareholders who acquire, or who are deemed to acquire, their ordinary shares by virtue of an office or employment. This summary is not exhaustive and shareholders should consult their own tax advisers as to the tax consequences in Ireland, or other relevant jurisdictions where we operate, including the acquisition, ownership and disposition of ordinary shares.

Withholding tax on dividends

While we have no current plans to pay dividends, dividends on our ordinary shares would generally be subject to Irish dividend withholding tax ("DWT") at the standard rate of income tax, which is currently 20%, unless an exemption

applies. Dividends on our ordinary shares that are owned by residents of the U.S. and held beneficially through the Depositary Trust Company ("DTC") will not be subject to DWT provided that the address of the beneficial owner of the ordinary shares in the records of the broker is in the U.S.

Dividends on our ordinary shares that are owned by residents of the U.S. and held directly (outside of DTC) will not be subject to DWT provided that the shareholder has completed the appropriate Irish DWT form and this form remains valid. Such shareholders must provide the appropriate Irish DWT form to our transfer agent at least seven business days before the record date for the first dividend payment to which they are entitled.

If any shareholder who is resident in the U.S. receives a dividend subject to DWT, he or she should generally be able to make an application for a refund from the Irish Revenue Commissioners on the prescribed form.

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Income tax on dividends

Irish income tax, if any, may arise in respect of dividends paid by us. However, a shareholder who is neither resident nor ordinarily resident in Ireland and who is entitled to an exemption from DWT, generally has no liability for Irish income tax or to the universal social charge on a dividend from us unless he or she holds his or her ordinary shares through a branch or agency in Ireland which carries out a trade on his or her behalf.

Irish tax on capital gains

A shareholder who is neither resident nor ordinarily resident in Ireland and does not hold our ordinary shares in connection with a trade or business carried on by such shareholder in Ireland through a branch or agency should not be within the charge to Irish tax on capital gains on a disposal of our ordinary shares.

Capital acquisitions tax

Irish capital acquisitions tax ("CAT") is comprised principally of gift tax and inheritance tax. CAT could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares are regarded as property situated in Ireland as our share register must be held in Ireland. The person who receives the gift or inheritance has primary liability for CAT.

CAT is levied at a rate of 33% above certain tax free thresholds. The appropriate tax free threshold is dependent upon (i) the relationship between the donor and the recipient, and (ii) the aggregation of the values of previous gifts and inheritances received by the recipient from persons within the same category of relationship for CAT purposes. Gifts and inheritances passing between spouses are exempt from CAT. Our shareholders should consult their own tax advisers as to whether CAT is creditable or deductible in computing any domestic tax liabilities.

Stamp duty

Irish stamp duty, if any, may become payable in respect of ordinary share transfers. However, a transfer of our ordinary shares from a seller who holds shares through DTC to a buyer who holds the acquired shares through DTC should not be subject to Irish stamp duty. A transfer of our ordinary shares (i) by a seller who holds ordinary shares outside of DTC to any buyer, or (ii) by a seller who holds the ordinary shares through DTC to a buyer who holds the acquired ordinary shares outside of DTC, may be subject to Irish stamp duty, which is currently at the rate of 1% of the price paid or the market value of the ordinary shares acquired, if greater. The person accountable for payment of stamp duty is the buyer or, in the case of a transfer by way of a gift or for less than market value, all parties to the transfer.

A shareholder who holds ordinary shares outside of DTC may transfer those ordinary shares into DTC without giving rise to Irish stamp duty provided that the shareholder would be the beneficial owner of the related book entry interest in those ordinary shares recorded in the systems of DTC, and in exactly the same proportions, as a result of the transfer and at the time of the transfer into DTC there is no sale of those book entry interests to a third party being contemplated by the shareholder. Similarly, a shareholder who holds ordinary shares through DTC may transfer those ordinary shares out of DTC without giving rise to Irish stamp duty provided that the shareholder would be the beneficial owner of the ordinary shares, and in exactly the same proportions, as a result of the transfer, and at the time of the transfer out of DTC there is no sale of those ordinary shares to a third party being contemplated by the shareholder. In order for the share registrar to be satisfied as to the application of this Irish stamp duty treatment where relevant, the shareholder must confirm to us that the shareholder would be the beneficial owner of the related book entry interest in those ordinary shares recorded in the systems of DTC, and in exactly the same proportions or vice versa, as a result of the transfer and there is no agreement for the sale of the related book entry interest or the

ordinary shares or an interest in the ordinary shares, as the case may be, by the shareholder to a third party being contemplated.

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Stock performance graph

The information contained in the performance graph below shall not be deemed to be “soliciting material” or to be “filed” with the SEC, and such information shall not be incorporated by reference into any future filing under the Securities Act or the Exchange Act, except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the cumulative total shareholder return on our ordinary shares from December 31, 2013 through December 31, 2018 with the cumulative returns of the Nasdaq Composite Total Return Index and the Nasdaq Biotechnology Index. The comparison assumes $100 was invested on December 31, 2013 in our ordinary shares and in each of the foregoing indices and further assumes reinvestment of any dividends. We did not declare or pay any dividends on our ordinary shares during the comparison period.

	Nine Months Ended December 31, 2013	Year Ended December 31, 2014	2015	2016	2017	2018
Alkermes	100	144	195	137	134	73
Nasdaq Composite Total Return	100	115	123	134	173	168
Nasdaq Biotechnology Index	100	134	149	117	142	128

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Item 6. Selected Financial Data

The selected historical financial data set forth below at December 31, 2018 and 2017 and for the years ended December 31, 2018, 2017 and 2016 are derived from our audited consolidated financial statements, which are included elsewhere in this Annual Report. The selected historical financial data set forth below at December 31, 2016 and for the years ended and at December 31, 2015 and 2014 are derived from audited consolidated financial statements, which are not included in this Annual Report.

The following selected consolidated financial data should be read in conjunction with our consolidated financial statements, the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in Item 7 of Part II of this Annual Report. The historical results are not necessarily indicative of the results to be expected for any future period.

	Year Ended December 31,				
(In thousands, except per share data)	2018	2017	2016	2015	2014
Consolidated Statements of Operations Data:					
REVENUES[1]:					
Manufacturing and royalty revenues	$526,675	$505,308	$487,247	$475,288	$516,876
Product sales, net	450,334	362,834	256,146	149,028	94,160
Research and development revenue	68,895	7,232	2,301	4,019	7,753
License revenue	48,370	28,000	—	—	—
Total revenues	1,094,274	903,374	745,694	628,335	618,789
EXPENSES:					
Cost of goods manufactured and sold	176,420	154,748	132,122	138,989	175,832
Research and development	425,406	412,889	387,148	344,404	272,043
Selling, general and administrative	526,408	421,578	374,130	311,558	199,905
Amortization of acquired intangible assets	65,168	62,059	60,959	57,685	58,153
Total expenses	1,193,402	1,051,274	954,359	852,636	705,933
OPERATING LOSS	(99,128)	(147,900)	(208,665)	(224,301)	(87,144)
OTHER (EXPENSE) INCOME , NET[2]	(27,839)	4,626	(5,722)	296	73,115
LOSS BEFORE INCOME TAXES	(126,967)	(143,274)	(214,387)	(224,005)	(14,029)
PROVISION (BENEFIT) FOR INCOME TAXES	12,344	14,671	(5,943)	3,158	16,032
NET LOSS	$(139,311)	$(157,945)	$(208,444)	$(227,163)	$(30,061)
LOSS PER ORDINARY SHARE:					
BASIC AND DILUTED	$(0.90)	$(1.03)	$(1.38)	$(1.52)	$(0.21)
WEIGHTED AVERAGE NUMBER OF ORDINARY SHARES OUTSTANDING:					
BASIC AND DILUTED	155,112	153,415	151,484	149,206	145,274
Consolidated Balance Sheet Data:					
Cash, cash equivalents and investments	$620,039	$590,716	$619,165	$798,849	$801,646
Total assets[3]	1,825,007	1,797,227	1,726,423	1,855,744	1,919,058
Long-term debt[3]	279,308	281,436	283,666	349,944	355,756
Shareholders' equity	1,171,285	1,202,808	1,209,481	1,314,275	1,396,837

(1) On January 1, 2018, we adopted the Financial Accounting Standards Board's ("FASB") Accounting Standards Codification ("ASC") 606, Revenue from Contracts with Customers ("Topic 606").

(2) 2015 includes a $9.6 million gain on the sale of the Company's Gainesville, GA manufacturing facility, the related manufacturing and royalty revenue associated with certain products manufactured at the facility, and the rights to IV/IM and parenteral forms of Meloxicam (the "Gainesville Transaction"). 2014 includes a gain on the sale of property, plant and equipment of $41.9 million, a gain on the sale of an investment in Civitas Therapeutics, Inc. of $29.6 million and a gain on the sale of an investment in Acceleron Pharma Inc. of $15.3 million.

(3) In 2015, the Company retrospectively adopted the FASB's guidance simplifying the presentation of debt issuance costs. As a result, deferred financing costs of $2.2 million that were classified within "Other long-term assets" at December 31, 2014 were reclassified to "Long-term debt" to conform to the then-current period presentation.

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Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following should be read in conjunction with our consolidated financial statements and related notes beginning on page F 1 of this Annual Report. The following discussion contains forward looking statements. Actual results may differ significantly from those projected in the forward looking statements. See "Cautionary Note Concerning Forward Looking Statements" on page 3 of this Annual Report. Factors that might cause future results to differ materially from those projected in the forward looking statements also include, but are not limited to, those discussed in "Item 1A—Risk Factors" and elsewhere in this Annual Report.

Overview

We earn revenue on net sales of VIVITROL, ARISTADA and ARISTADA INITIO, which are proprietary products that we manufacture, market and sell in the U.S., and manufacturing and/or royalty revenues on net sales of products commercialized by our licensees. Our key marketed products are expected to generate significant revenues for us in the near and medium term and we believe are singular or competitively advantaged products in their classes. In 2018, these key marketed products consisted of VIVITROL; ARISTADA and ARISTADA INITIO; INVEGA SUSTENNA/XEPLION, INVEGA TRINZA/TREVICTA; RISPERDAL CONSTA; and AMPYRA/FAMPYRA. Revenues from these key products accounted for 80% of our total revenues during 2018, as compared to 86% during 2017 and 2016.

In 2018, we incurred an operating loss of $99.1 million, as compared to $147.9 million in 2017. Revenues increased by 21% in 2018, as compared to 2017, which was primarily due to revenue earned under our license and collaboration agreement with Biogen for BIIB098 and increased sales of ARISTADA. This was partially offset by a 14% increase in operating expenses, which were primarily in support of the increase in sales of our proprietary products and continued investment in our R&D pipeline and commercial organization. These items are discussed in further detail within the Results of Operations section below.

Results of Operations

Manufacturing and Royalty Revenues

Manufacturing revenues for products that incorporate our technologies, except for those from Janssen related to RISPERDAL CONSTA, are recognized over time as products move through the manufacturing process, using an input method based on costs as a measure of progress. Manufacturing revenue from RISPERDAL CONSTA is recognized at the point in time the product has been fully manufactured. Royalties are generally earned on our licensees' net sales of products that incorporate our technologies and are recognized in the period the products are sold by our licensees. The following table compares manufacturing and royalty revenues earned in the years ended December 31, 2018, 2017 and 2016:

				Change	
	Year Ended December 31,			Favorable/(Unfavorable)	
(In millions)	2018	2017	2016	2018–2017	2017–2016
Manufacturing and royalty revenues:					
INVEGA SUSTENNA/XEPLION & INVEGA TRINZA/TREVICTA	$241.4	$214.9	$184.2	$ 26.5	$ 30.7
AMPYRA/FAMPYRA	107.1	117.0	114.2	(9.9)	2.8

RISPERDAL CONSTA	71.1	84.9	87.2	(13.8)	(2.3)
Other	107.1	88.5	101.6	18.6	(13.1)
Manufacturing and royalty revenues	$526.7	$505.3	$487.2	$ 21.4	$ 18.1

Under our INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA agreement with Janssen, we earn royalties on end market net sales of INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA of 5% up to the first $250 million in calendar year sales, 7% on calendar year sales of between $250 million and $500 million, and 9% on calendar-year sales exceeding $500 million. The royalty rate resets at the beginning of each calendar year to 5%. The increase in INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA royalty revenues in each period was due to an increase in Janssen's end market net sales of INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA. Janssen's end market net sales of INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA were $2.9 billion, $2.6 billion and $2.2 billion during the years ended December 31, 2018, 2017 and 2016, respectively. The adoption of Topic 606 had no impact on the method in which we recognize royalty revenue from sales of INVEGA SUSTENNA/XEPLION and INVEGA TRINZA/TREVICTA.

Under Topic 606, we recognize manufacturing revenue, equal to 7.5% of Janssen's unit net sales price of RISPERDAL CONSTA, at the point in time when RISPERDAL CONSTA has been fully manufactured, which is when the product is approved for shipment. Prior to the adoption of Topic 606 we recognized manufacturing revenue when RISPERDAL CONSTA was shipped to Janssen. We continue to record royalty revenue, equal to 2.5% of end-market net sales, when the end-market sale of RISPERDAL CONSTA occurs.

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The decrease in RISPERDAL CONSTA revenue in 2018, as compared to 2017, was due to a 19% decrease in manufacturing revenue and a 9% decrease in royalty revenue. The decrease in manufacturing revenues was due to a 19% decrease in the number of units of RISPERDAL CONSTA manufactured for Janssen. The decrease in royalty revenue was due to a decline in Janssen's end-market net sales of RISPERDAL CONSTA. Janssen's end market net sales of RISPERDAL CONSTA were $737.0 million, $805.0 million and $893.0 million during the years ended December 31, 2018, 2017 and 2016, respectively. The decrease in RISPERDAL CONSTA revenue in 2017, as compared to 2016, was primarily due to a 10% decrease in royalty revenues due to the decline in Janssen's end-market net sales of RISPERDAL CONSTA. RISPERDAL CONSTA is covered by a patent until 2021 in the EU and 2023 in the U.S. For a discussion of legal proceedings related to this patent, see Note 16, Commitments and Contingent Liabilities in the "Notes to Consolidated Financial Statements" and "Item 3—Legal Proceedings" in this Annual Report, and specifically the section entitled "—We or our licensees may face claims against intellectual property rights covering our products and competition from generic drug manufacturers."

We expect revenues from our long acting, atypical antipsychotic franchise to continue to grow as INVEGA SUSTENNA/XEPLION grows and INVEGA TRINZA/TREVICTA is launched around the world. A number of companies, including us, are working to develop products to treat schizophrenia and/or bipolar disorder that may compete with INVEGA SUSTENNA/XEPLION, INVEGA TRINZA/TREVICTA and RISPERDAL CONSTA. Increased competition may lead to reduced unit sales of INVEGA SUSTENNA/XEPLION, INVEGA TRINZA/TREVICTA and RISPERDAL CONSTA, as well as increasing pricing pressure. The latest of the patents subject to our license agreement with Janssen covering INVEGA SUSTENNA/XEPLION expires in 2030 in the U.S. and certain other countries and in 2022 in the EU. The latest of the licensed patents covering INVEGA TRINZA/TREVICTA expired in 2017 in the U.S. and will expire in 2022 in the EU. In addition, Janssen has other patents not subject to our license agreement, including one that covers INVEGA SUSTENNA in the U.S. and expires in 2031 and one that covers INVEGA TRINZA in the U.S. and expires in 2036.

In January 2018, Janssen Pharmaceuticals NV and Janssen Pharmaceuticals, Inc. initiated a patent infringement lawsuit in the U.S. District Court for the District of New Jersey against Teva, who filed an ANDA seeking approval to market a generic version of INVEGA SUSTENNA before the expiration of U.S. Patent No. 9,439,906. For further discussion of the legal proceedings related to the patents covering INVEGA SUSTENNA, see Note 16, Commitments and Contingent Liabilities in the "Notes to Consolidated Financial Statements" and "Part I, Item 3—Legal Proceedings" in this Annual Report and for information about risks relating to the INVEGA SUSTENNA Paragraph IV litigation, see "Part I, Item 1A—Risk Factors" in this Annual Report, and specifically the section entitled "—We or our licensees may face claims against intellectual property rights covering our products and competition from generic drug manufa