UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

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

For the fiscal year ended December 31, 2019

OR

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

Commission File Number 001-35892

GW PHARMACEUTICALS PLC

(Exact name of Registrant as specified in its charter)

England and Wales (State or other jurisdiction of incorporation or organization)	**Not Applicable** (I.R.S. Employer Identification No.)
Sovereign House, Vision Park Chivers Way, Histon Cambridge, CB24 9BZ United Kingdom (Address of principal executive offices)	**+44 1223 266800** (Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol	Name of exchange on which registered
American Depositary Shares, each representing 12 Ordinary Shares, par value £0.001 per share	**GWPH**	**The Nasdaq Global Market**

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

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

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

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

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2019, the last business day of the Registrant's most recently completed second fiscal quarter was approximately $5,165,756,855.

As of February 21, 2020, 371,731,604 shares were outstanding including 358,636,068 shares held as American Depositary Shares, each representing twelve Ordinary Shares, par value £0.001 per share and 13,095,536 Ordinary Shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement to be used in connection with the solicitation of proxies for the Registrant's 2020 Annual Meeting of Shareholders are incorporated by reference in Part III of this Annual Report on Form 10-K.

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PART I

INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This annual report on Form 10-K (Annual Report) contains forward-looking statements that are based on our current expectations, assumptions, estimates and projections about us and our industry. All statements other than statements of historical fact in this Annual Report are forward-looking statements

These forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors that could cause our actual results of operations, financial condition, liquidity, performance, prospects, opportunities, achievements or industry results, as well as those of the markets we serve or intend to serve, to differ materially from those expressed in, or suggested by, these forward-looking statements. These forward-looking statements are based on assumptions regarding our present and future business strategies and the environment in which we expect to operate in the future. Important factors that could cause those differences include, but are not limited to:

- the inherent uncertainty of product development;
- successful commercialization and marketing of Epidiolex or Epidyolex (the trade name for Epidiolex in Europe) and market acceptance of Epidiolex/Epidyolex;
- our and our contract manufacturers' ability to successfully manufacture commercial quantities of our products in compliance with regulatory requirements;
- our ability to establish and maintain commercialization organizations in the U.S., Europe and elsewhere;
- our ability to submit and maintain Investigational New Drug applications, or INDs, and New Drug Applications, or NDAs, with the U.S. Food and Drug Administration, or the FDA, and comparable filings outside of the U.S.;
- our ability to successfully design, commence and complete clinical trials;
- our ability to receive and maintain regulatory exclusivities, including Orphan Drug Designations for our drugs and our drug candidates;
- patents, including, but not limited to, our ability to have patents issued covering our drugs, drug candidates and processes, as well as oppositions and legal challenges;
- government regulation and approvals;
- future revenue being lower than expected;
- the level of pricing and reimbursement for our products and product candidates, if approved;
- increasing competitive pressures in our industry;
- general economic conditions or conditions affecting demand for the products offered by us in the markets in which we operate, both domestically and internationally, being less favorable than expected;
- currency fluctuations and hedging risks;
- worldwide economic and business conditions and conditions in the industry in which we operate;
- our relationships with our customers and suppliers;
- increased competition from other companies in the industry in which we operate;
- changing technology;

- our ability to manage and maintain our applications and data systems from security breaches and data loss;
- claims for personal injury or death arising from the use of products and product candidates produced by us;
- the occurrence of accidents or other interruptions to our production processes;
- changes in our business strategy or development plans, and our expected level of capital expenses;
- our ability to attract and retain qualified personnel, including with respect to the commercialization of Epidiolex;
- regulatory, environmental, legislative and judicial developments;
- our intention not to pay dividends; and
- factors that are not known to us at this time.

Additional factors that could cause actual results, financial condition, liquidity, performance, prospects, opportunities, achievements or industry results to differ materially include, but are not limited to, those discussed under "Risk Factors" in Part I, Item 1A in this Annual Report and in our other filings with the U.S. Securities and Exchange Commission (the "SEC"). Additional risks that we may currently deem immaterial or that are not presently known to us could also cause the forward-looking events discussed in this Annual Report not to occur. The words "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect" and similar words are intended to identify estimates and forward-looking statements. Estimates and forward-looking statements speak only at the date they were made, and we undertake no obligation to update or to review any estimate and/or forward-looking statement because of new information, future events or other factors. Estimates and forward-looking statements involve risks and uncertainties and are not guarantees of future performance. Our future results may differ materially from those expressed in these estimates and forward-looking statements. In light of the risks and uncertainties described above, the estimates and forward-looking statements discussed in this Annual Report might not occur, and our future results and our performance may differ materially from those expressed in these forward-looking statements due to, inclusive of, but not limited to, the factors mentioned above. Because of these uncertainties, you should not make any investment decision based on these estimates and forward-looking statements.

GENERAL INFORMATION

In this Annual Report, "GW Pharma," the "Group," the "Company," "we," "us" and "our" refer to GW Pharmaceuticals plc and its consolidated subsidiaries, except where the context otherwise requires.

Epidiolex®, Epidyolex® (the European trade name for Epidiolex), and Sativex® are registered trademarks of GW Pharmaceuticals plc. Nabiximols is the U.S. adopted name for Sativex, and Sativex will be referred to as "nabiximols" throughout this Annual Report, except where the context requires otherwise.

Item 1. Business

Company Overview

We are a biopharmaceutical company focused on discovering, developing and commercializing novel therapeutics from our proprietary cannabinoid product platform in a broad range of disease areas. In over 20 years of operations, we have established a world leading position in the science, development and commercialization of plant-derived cannabinoid therapeutics through our proven drug discovery and development processes, our intellectual property portfolio, regulatory, manufacturing and commercial expertise.

Our lead cannabinoid product is Epidiolex, a pharmaceutical formulation of cannabidiol, or CBD, for which we retain global commercial rights. Epidiolex is approved in the United States for the treatment of seizures associated with Lennox-Gastaut syndrome, or LGS, and Dravet syndrome, in patients two years of age and older. LGS and Dravet syndrome are severe childhood-onset, drug-resistant epilepsy syndromes. We launched Epidiolex in the United States in November 2018. In September 2019, we received approval from the European Commission, or EC, for Epidyolex (the trade name in Europe for Epidiolex) for use as adjunctive therapy of seizures associated with LGS or Dravet syndrome, in conjunction with clobazam, for patients two years of age and older. We have launched Epidyolex in Germany and the U.K. and are planning launches in France, Italy and Spain during 2020.

We continue to develop Epidiolex for additional indications. In May 2019, we announced positive results from a Phase 3 trial for the use of Epidiolex to treat seizures associated with Tuberous Sclerosis Complex, or TSC, a rare genetic disorder that causes non-malignant tumors to form in many different organs that affects approximately 50,000 individuals in the United States and one million worldwide. On February 3, 2020, we announced that we had submitted a supplemental New Drug Application, or sNDA, to the FDA to expand the Epidiolex label to include the treatment of seizures associated with TSC. We expect to file for supplemental approval for the TSC indication in Europe in the first quarter of 2020. We have received Orphan Drug Designation from the FDA and the Committee for Orphan Medical Products (COMP) for TSC (we previously received the same designations for Dravet syndrome and LGS).

We have begun recruiting patients for a pivotal trial of Epidiolex in the treatment of Rett syndrome, a rare, non-inherited neurodevelopmental disorder affecting approximately one in 10,000 to 15,000 live female births. This trial focuses on the behavioral abnormalities associated with the disorder.

We have a deep pipeline of additional cannabinoid product candidates that includes compounds in Phase 1, Phase 2, and Phase 3 trials. Our most advanced pipeline asset in the United States is nabiximols, for which we expect to commence a pivotal clinical program in the first half of 2020 in the treatment of spasticity due to multiple sclerosis. We anticipate commercializing nabiximols in the U.S. using our in-house commercial organization. Nabiximols is already approved in over 25 countries outside the United States for the treatment of spasticity due to multiple sclerosis under the brand name Sativex. We are advancing plans to commence clinical programs for nabiximols in 2020 in spasticity due to spinal cord injury and post-traumatic stress disorder, or PTSD.

In addition to nabiximols, our pipeline includes cannabinoid product candidates for schizophrenia, autism spectrum disorder, or ASD, and Neonatal Hypoxic Ischemic Encephalopathy, or NHIE.

Our Marketed Products

Epidiolex

Epidiolex in the U.S.

We launched Epidiolex on November 1, 2018 in the U.S. market after FDA approval for the treatment of seizures associated with LGS or Dravet syndrome in patients two years of age and older. The FDA confirmed orphan drug exclusivity for Epidiolex and granted us a rare pediatric disease voucher. Following the approval, the U.S. Drug Enforcement Administration, or DEA, placed Epidiolex in Schedule V.

Our U.S. subsidiary, Greenwich Biosciences, Inc., markets Epidiolex through a commercial organization consisting of sales, medical affairs, marketing, and market access/payer teams.

The U.S. sales team includes two National Directors, eight Regional Managers and 65 Neurology Account Managers and is targeting approximately 6,400 physicians who treat patients with LGS or Dravet syndrome. In 2020, we will be launching a commercial initiative in the long-term care segment.

We set a list price for Epidiolex of $1,235 per 100mL bottle at the time of launch in November 2018, and a list price of $1,310 per 100mL bottle effective as of January 4, 2020. Our patient support programs provide patient and caregiver focused education and help provide resources that may lower patients' out-of-pocket costs or provide product at no cost to eligible patients. In addition, a number of national payers have now established favorable coverage policies for Epidiolex.

Epidyolex in Europe

On September 23, 2019, we announced that the EC approved the marketing authorization for Epidyolex (the trade name in Europe for Epidiolex) for use as adjunctive therapy of seizures associated with LGS or Dravet syndrome, in conjunction with clobazam, for patients two years of age and older. We have launched Epidyolex in Germany and the U.K. and are planning launches in France, Italy and Spain during 2020.

Epilepsy Market Overview

According to the Epilepsy Foundation, approximately 3.4 million people in the U.S. live with epilepsy. According to Kwan and Brodie in the February 2000 edition of *The New England Journal of Medicine*, 36 percent of patients with epilepsy were pharmaco-resistant even after the use of three anti-epilepsy drugs (AEDs). Furthermore, it is recognized that some of those that do find relief often suffer side effects severe enough with their current medication that an alternative or adjunct treatment is often sought. The costs of uncontrolled epilepsy are significant, with direct and indirect costs associated with epilepsy totaling more than $15 billion per year. It is estimated that 50,000 epilepsy related deaths occur each year, more than breast cancer deaths annually.

According to Russ et al. in the February 2012 edition of Pediatrics, there are 466,000 childhood epilepsy patients in the U.S. and 765,000 patients in Europe, of which 30 percent, or about 140,000 patients in the U.S. and about 230,000 in Europe, are deemed medically intractable or pharmaco-resistant.

Dravet Syndrome

Dravet syndrome is a severe form of infantile-onset, genetic, drug-resistant epilepsy with a distinctive but complex electroclinical presentation. The clinical onset of Dravet syndrome occurs during the first year of life with clonic seizures (jerking) and tonic-clonic (convulsive) seizures in previously healthy and developmentally normal infants often associated with a high fever. Symptoms peak at about five months of age, and the latest onset beginning by 15 months of age. Other seizures develop between one and four years of age such as prolonged focal dyscognitive seizures and brief absence seizures. The duration of these seizures decreases during this period, while their frequency increases. Prognosis is poor, with death occurring in approximately 14 percent of children. Death can be caused by the seizures themselves, by infection due to prolonged periods of physical inactivity, or by the presence of advanced neurodegenerative disease or a compromised level of consciousness. Death can also occur suddenly due to uncertain causes, often because of the relentless neurological decline or from Sudden Unexpected Death in Epilepsy. Patients develop intellectual disability and life-long ongoing seizures. Intellectual impairment varies from severe (50 percent of patients), to moderate (25 percent of patients), to mild (25 percent of patients). Patients rarely return to normal intellect.

According to Forsgren L. et al. in the 2004 edition of *Epilepsy in Children*, the incidence of epilepsy in the first year of life is 1.5 per 1,000 people, or, by our estimate, 6,450 new epilepsies per year worldwide. According to Dravet et al. in the 2012 edition of *Epileptic Syndromes in Infancy, Childhood and Adolescence*, up to 5 percent of epilepsies diagnosed in the first year of life are Dravet syndrome, equating to 320 new cases per year in the U.S. with a mortality rate that may be as high as 15 percent in the first 20 years of life. By our estimate, there are approximately 5,440 patients with Dravet syndrome in the U.S. under the age of 20 years. Applying the same assumptions in Europe, we believe there are an estimated 6,710 Dravet syndrome patients in the European Union under the age of 20 years.

A large percentage of cases of Dravet syndrome have a family history of epilepsy or convulsions. Heterozygous de novo mutations of the alpha 1 (α-1) subunit of the SCN1A gene, which encodes a voltage-gated sodium channel, are the cause of Dravet syndrome in 75 percent to 80 percent of patients and more than 500 SCN1A mutations have been reported to be associated with this disorder. The standard of care usually involves a combination of the following anticonvulsants: clobazam, clonazepam, leviteracetam, topirimate, valproic acid, ethosuximide or zonisamide. Stiripentol is approved for the treatment of Dravet syndrome in conjunction with clobazam and valproate. Several reports suggest that potent sodium channel blockers used to treat epilepsy actually increase seizure frequency in patients with Dravet syndrome. The most common of which are phenytoin, carbamazepine, lamotrigine and rufinamide. Management of this disease may also include a ketogenic diet, and physical and communication therapy. In addition to anti-convulsive drugs, many patients with Dravet syndrome are treated with anti-psychotic drugs, stimulants or drugs to treat insomnia.

Lennox-Gastaut Syndrome

LGS is a type of epilepsy with multiple types of seizures, particularly tonic (stiffening) and atonic (drop) seizures. According to Trevathan et al. in the December 1997 edition of *Epilepsia*, the estimated prevalence of LGS is between 3 percent and 4 percent of childhood epilepsy cases. LGS affects between 14,500 to 18,500 children under the age of 18 years in the U.S. and over 30,000 children and adults in the U.S. Eighty percent of children with LGS continue to experience seizures, psychiatric, intellectual and behavioral deficits in adulthood. Seizures due to LGS are hard to control and generally require life-long treatment.

Drug resistance is one of the main features of LGS. Generally, treatment requires broad spectrum AEDs and almost always polypharmacy. Treatment also depends on the seizure type as some treatments effective for one type of seizure may worsen another. The FDA approved treatments for LGS in addition to Epidiolex are: Onfi (clobazam); Banzel (rufinamide); Lamictal (lamotrigine); Topamax (topirimate); and Felbatol (felbamate). These medicines are often used as adjunctive therapy with other AEDs and they show some efficacy, however, many also have severe undesirable side effects. Furthermore, several of these medicines are based on the same mechanism of action as traditional AEDs. As patients with LGS generally need to take several treatments to gain any change to their seizure frequency, we believe that there remains a need for further pharmacological treatments, particularly those with a different mechanism of action, to give prescribers more options in treating this rare, pharmacoresistant syndrome.

Epidiolex Follow-On Target Indication: TSC

In early February 2020, we submitted an sNDA to the FDA to expand the Epidiolex label to include the treatment of seizures associated with TSC. TSC is a genetic disorder that causes non-malignant tumors to form in many different organs, primarily in the brain, eyes, heart, kidney, skin and lungs. The brain and skin are the most affected organs. TSC results from a mutation in tumor suppression genes TSC1 or TSC2. According to the Tuberous Sclerosis Alliance, TSC is estimated to affect approximately 50,000 patients in the U.S. The most common symptom of TSC is epilepsy, which occurs in 75 – 90 percent of patients, about 70 percent of whom experience seizure onset in their first year of life. TSC patients typically have treatment-resistant seizures. The seizures of TSC are typically focal in onset, meaning that they are localized to one region and hemisphere of the brain. There are significant co-morbidities associated with TSC including cognitive impairment in 50 percent, ASD in up to 40 percent and neurobehavioral disorders in over 60 percent of individuals with TSC.

In May 2019, we announced positive top-line Phase 3 results in the use of Epidiolex to treat seizures associated with TSC, and more extensive study results from this positive trial were presented in December 2019 at the annual meeting of the American Epilepsy Society. This dose-ranging trial was a 16-week comparison of Epidiolex versus placebo to assess the safety and efficacy of Epidiolex as an adjunctive anti-epileptic treatment. The primary measure of this trial was the percentage change from baseline in seizure frequency during the treatment period. Primary endpoint seizure types included focal motor seizures with or without impairment of consciousness or awareness and generalized convulsive seizures. The study found that patients treated with Epidiolex 25 mg/kg/day or 50 mg/kg/day experienced a significantly greater reduction in TSC-associated seizures (49% for 25 mg/kg/day and 48% for 50 mg/kg/day) compared to placebo (27%; p=0.0009 and p=0.0018, respectively) and secondary endpoint data showed that more patients on Epidiolex experienced a 50% or greater reduction in seizures (36% for 25 mg/kg/day and 40% for 50 mg/kg/day) compared to placebo (22%; p=0.0692 and p=0.0245, respectively). The safety profile observed was consistent with findings from previous studies, with no new safety risks identified.

Epidiolex Follow-On Target Indication: Rett Syndrome

Rett syndrome, or RTT, is a rare, non-inherited, X-linked neurodevelopmental disorder affecting approximately 1 in 10,000 to 15,000 live female births. RTT is most commonly caused by heterozygous de-novo mutations in the gene encoding methyl-CpG-binding protein 2, or MeCP2, resulting in a loss of function of the MeCP2 protein. The condition affects predominantly females and it results in abnormal neuronal development and function in affected children. The symptomatology of RTT is progressive, with early onset from about 6–18 months of life, followed by a rapid destructive phase at the age of 1 to 4 years. This stage is characterized by loss of purposeful hand skills, loss of spoken language, breathing and cardiac irregularities, microcephaly, and autistic-like behaviors. After the period of regression, patients enter a prolonged period of stabilization where most of the impairments associated with the destructive phase persist together with apraxia, motor problems, and seizures. Over time, the patient's motor function continues to deteriorate, resulting in reduced mobility, scoliosis, rigidity, muscular weakness and spasticity.

There are no approved treatments for RTT. The management options target specific symptoms and are not without undesirable side effects. As such, there is currently a high unmet medical need. Data from animal models suggest CBD may be able to improve deficits in cognition, language, social behavior and motor function, as well as having the potential to modulate the cellular mechanisms thought to be involved in the neurobehavioral deficits present in RTT. In addition, reports from open label investigations in patients with refractory epilepsy suggest that Epidiolex may have beneficial effects on cognition, behavior and quality of life, which could benefit patients with RTT.

A Phase 3 trial of Epidiolex in patients with RTT was initiated in 2019 and is an international multi-center, randomized, double-blind, placebo-controlled study. The endpoints are to evaluate the efficacy of up to 24 weeks of treatment with Epidiolex, compared with placebo, in reducing symptom severity in patients with RTT using the Rett Syndrome Behavior Questionnaire and the Clinical Global Impressions - Improvement.

Epidiolex Formulation Life Cycle Management

In addition to the currently marketed Epidiolex oral solution formulation, we continue to develop additional formulations of CBD as part of its life cycle management plan. We are developing a capsule to provide more convenient administration, particularly for adults and older children across our target indications. We are also developing an improved oral solution.

Epidiolex Intellectual Property and Other Protections

In addition to seven years of orphan exclusivity plus the potential six-month pediatric extension (to be filed), we seek to protect Epidiolex through the expansion of our patent portfolio. Our patent portfolio relating to the use of CBD in the treatment of epileptic encephalopathies includes 34 distinct patent families that are either granted or filed. Most of the patent families in this portfolio claim the use of CBD in the treatment of particular childhood epilepsy syndromes, seizure sub-types and interactions with other concomitantly dosed anti-seizure drugs. To date, we have obtained twelve patents and received notices of allowance for a further two from the U.S. Patent and Trademark Office, or USPTO, including claims for the use of CBD for the treatment of convulsive, drop and atonic seizures associated with both LGS and Dravet syndrome, as well as the use of CBD with clobazam, and the teaching that dose adjustment may be needed when concomitantly prescribed. Some of these patents are directly aligned with the Epidiolex label, and we have listed them in the Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book). These patents have expiry to 2035. We recently filed an international patent application based on promising data that we believe demonstrates that Epidiolex is more efficacious than synthetic CBD at the same concentration in a mouse model of seizures. Unlike synthetic CBD, Epidiolex comprises up to 2% of other cannabinoids. It would appear from this early data that the presence of these cannabinoids, albeit in small amounts, provides an additional benefit over CBD alone in an animal model of epilepsy. This patent, if granted, will have an expiry date of 2039. We continue to identify novel findings and submit patent applications resulting from the Epidiolex development program and we expect additional grants from these applications.

Nabiximols (known as Sativex outside the U.S.)

Nabiximols is a complex botanical medicine formulated from extracts of the cannabis sativa plant that contains the principal cannabinoids delta-9-tetrahydrocannabinol, or THC, and CBD as well as specific minor cannabinoids and other non-cannabinoid components. We developed nabiximols to be administered as an oromucosal spray, whereby the active ingredients are absorbed in part in the lining of the mouth, either under the tongue or inside the cheek. Nabiximols is already approved in over 25 countries outside the United States for the treatment of spasticity due to multiple sclerosis under the brand name Sativex. To support the development and commercialization of Sativex internationally, we have license and development agreements with commercial partners. These agreements provide our collaborators with the sole right to commercialize Sativex in exclusive territories for all indications.

The development of nabiximols in the United States is described below under "Our Product Pipeline."

Nabiximols Intellectual Property and Other Protections

Our strategy is to seek and obtain patents related to nabiximols across all major pharmaceutical markets around the world. In the U.S., our patents (and our pending applications if they issue) relating to nabiximols would expire on various dates between 2021 and 2029, excluding possible patent term extensions. We have at least seven different patent families containing one or more pending and/or issued patents directed to the nabiximols formulation, the medical use of nabiximols, the extracts from which nabiximols is composed, the extraction technique used to produce the extracts and the therapeutic use of nabiximols. Due to the product's significant complexity, we believe that nabiximols will benefit from strong long-term market regulatory protection.

Our Product Pipeline

Proprietary Cannabinoid Product Platform

The cannabis plant is the unique source of more than 70 structurally related, plant-derived cannabinoids. Although one cannabinoid, THC, is known to cause psychoactive effects associated with the use of illicit herbal cannabis, none of the other cannabinoids are known to share this property. In recent decades, there have been major scientific advances that have led to the discovery of new plant-derived cannabinoids and their potential for therapeutic use. We are a global leader in this developing area of science, and we believe that our proprietary cannabinoid product platform uniquely positions us to discover and develop cannabinoids as new therapeutics.

Our proprietary cannabinoid product platform consists of our:

- continually evolving library of internally generated novel cannabis plant types that produce selected cannabinoids, or chemotypes. We can reproduce the selected chemotypes through propagation of plant cuttings, or clones, in order to ensure that all subsequent plant material is genetically uniform. We can also generate seeds of selected chemotypes for large-scale production;
- in-house extraction, processing methodologies and analytical techniques, which yield well-characterized and standardized chemotype extracts;
- discovery of novel cannabinoid pharmacology through conducting *in vitro* and *in vivo* pharmacologic evaluation studies in validated disease models to determine the most promising potential therapeutic areas for each cannabinoid or extract;
- in-house formulation and manufacturing capabilities, supplemented by third-party contractors;
- global in-house development and regulatory expertise; and
- intellectual property portfolio, which includes issued and/or pending claims directed to plants, plant extracts, extraction technology, pharmaceutical formulations, drug delivery and the therapeutic uses of cannabinoids, as well as plant variety rights, know-how and trade secrets.

With the exception of Sativex, which is subject to licensing agreements described above outside of the United States, we retain global commercial rights to all of our product pipeline candidates.

Pipeline Summary

Product/Product Candidates	Indication	Partner(s)	Status	Expected Next Steps
Epidiolex (CBD)	Childhood-onset epilepsy	We retain global rights.		
	Initial targets: Treatment of seizures in LGS and Dravet syndrome in patients two years of age and older		Approved by the FDA and launched in the U.S. Approved by the EC (under the brand name Epidyolex).	
	Additional targets: TSC		Positive Phase 3 trial completed. Supplemental NDA filed in February 2020.	
	Rett syndrome		Phase 3 trial in Rett initiated.	
Nabiximols	MS spasticity (ex- U.S.)	Almirall, Bayer, Ipsen and Neopharm	Approved in numerous countries.	
	MS spasticity (U.S.)	We retain rights.	FDA meetings held to determine pivotal clinical program.	Pivotal clinical trials to commence in 2020.
	Spasticity associated with Spinal Cord Injury		Planning Phase 2/3 trial.	Initiate Phase 2/3 trial.
	Post-Traumatic Stress Disorder		Planning Phase 2 trial.	Initiate Phase 2 trial.
	Other neurological symptoms		Evaluating next target indications	
GWP42003	Schizophrenia	We retain global rights.	Positive Phase 2 proof-of-concept.	Phase 2b trial to commence in 2020.
GWP42006 (CBDV)	Autism Spectrum Disorder	We retain global rights.	Company sponsored open-label trial commenced. Investigator-led placebo-controlled trial in autism; expanded access IND to treat seizures associated with autism commenced in 2019.	
	Rett syndrome		Investigator-led Phase 2 open label trial in Rett syndrome. Trial initiated in 2019. FDA orphan designation in Rett syndrome.	
	Epilepsy		Phase 2a trial completed.	Under evaluation.
Intravenous GWP42003	Neonatal hypoxic-ischemic encephalopathy	We retain global rights.	Recruiting for Phase 2 trial in neonates.	

Nabiximols in the United States

Our nearest term pipeline opportunity in the United States is nabiximols. Following meetings with the FDA, we expect to commence a pivotal clinical program in 2020 for nabiximols in the treatment of spasticity due to multiple sclerosis. We believe that nabiximols has the potential to be developed in several additional indications and are planning clinical programs in spasticity due to spinal cord injury and PTSD.

MS is the most common disabling neurological condition affecting young adults. According to the World Health Organization, MS affects more than 1.3 million people worldwide, of which over 400,000 are in the United States and over 600,000 are in Europe. MS affects twice as many women as men and typically develops between the ages of 20 and 40 years. Spasticity is one of the most common, chronic, and disabling symptoms of MS, affecting up to 80% of MS patients over their lifetimes. Spasticity refers to an abnormal, involuntary tightness of muscles, which increases when the muscles are rapidly stretched, so that the associated joint appears to resist movement. Some of the features of spasticity include muscle stiffness, muscle spasms and pain. As a result of the increased muscle tone due to spasticity, “simple” everyday movements become difficult or impossible altogether. In addition, painful muscle spasms can lead to difficulty with sleeping, sitting in a chair or lying in bed. Occasionally, spasms may be triggered by fairly minor irritations such as tight clothing, a full bladder or bowel, urinary tract infection or skin irritation, such as from a pressure sore. Moderate to severe spasticity can lead to significant impairment.

There is no cure for MS spasticity, and it is widely recognized that currently available oral treatments afford only partial relief and have clinically-important side effects. Nabiximols offers the prospect of treating U.S. patients who might otherwise require invasive and costly alternative treatment options such as intrathecal baclofen or surgery. Because nabiximols has been approved and commercialized elsewhere around the world since 2005, we have collected nearly 100,000 patient years of safety data and believe its safety profile has been well established.

With respect to the lifecycle for nabiximols beyond MS spasticity, we see potential opportunities within the broader spasticity markets as there are around three million patients in the United States with spasticity associated with various conditions. We are, in parallel, planning clinical programs in two further indications, spasticity due to spinal cord injury and PTSD. We expect to commence clinical programs in the second half of 2020 to address these broader markets with a view to achieving a series of approved indications for nabiximols over the coming years.

GWP 42003 in Schizophrenia

Schizophrenia is a chronic disease that manifests through disturbances of perception, thought, cognition, emotion, motivation and motor activity. Over a lifetime, about 1 percent of the population will develop schizophrenia. All antipsychotic treatments for schizophrenia rely primarily upon their antagonistic action at the dopamine D2 receptor for their antipsychotic effect. They produce a wide range of adverse events and are often poorly tolerated by patients resulting in poor compliance with treatment. Current antipsychotics also have little or no effect upon the negative symptoms (blunted mood and lack of pleasure, motivation and movement) of schizophrenia or the associated cognitive deficit. Furthermore, the positive symptoms (such as hallucinations, delusions and thought disorder) of at least one-third of patients fail to respond adequately to current treatments.

GWP42003 features CBD as the primary cannabinoid and has shown notable anti-psychotic effects in accepted pre-clinical models of schizophrenia and importantly has also demonstrated the potential to reduce the characteristic movement disorders induced by currently available anti-psychotic agents. In September 2015, we announced positive top line results from an exploratory Phase 2 placebo-controlled clinical trial of GWP42003 in 88 patients with schizophrenia who had previously failed to respond adequately to first line anti-psychotic medications. Over a series of exploratory endpoints, GWP42003 was consistently superior to placebo, with the most notable differences being in the PANSS positive sub-scale ($p=0.019$), the Clinical Global Impression of Severity ($p=0.04$) and Clinical Global Impression of Improvement ($p=0.018$). The safety profile of GWP42003 was reassuring, with no serious adverse events and an overall frequency of adverse events similar to placebo. This study was published in the *American Journal of Psychiatry* in December 2017.

We are commencing a Phase 2b trial of GWP42003 in Schizophrenia in the first half of 2020.

Our portfolio of intellectual property related to the use of cannabinoids in schizophrenia includes a number of issued patents and pending applications in both the U.S. and Europe. This portfolio is directed to the use of various cannabinoids individually or in combination with other cannabinoids or antipsychotic medications in the treatment of schizophrenia or side effects relating to schizophrenia.

GWP42006 (CBDV) in Epilepsy, Rett and Autism Spectrum Disorder

GWP42006 features CBDV as the primary cannabinoid. CBDV has shown anti-epileptic properties across a range of *in vitro* and *in vivo* models of epilepsy.

We have also evaluated GWP42006 in both general and syndromic pre-clinical models of ASD yielding promising signals on cognitive and social endpoints as well as repetitive behavior. These animal models include both genetically determined abnormalities of neurobehavioral, and chemically-induced models, and include Rett syndrome and Fragile X syndrome among others. Many of the pediatric intractable epilepsy conditions within the Epidiolex expanded access program share considerable overlap with ASD and these conditions often fall within the orphan disease space. Initial clinical observations from treating physicians suggest a potential role for cannabinoids in addressing problems associated with ASD such as deficits in cognition, behavior and communication.

We are working on various clinical initiatives for CBDV in the field of autism spectrum disorder, or ASD. We initiated a company-sponsored open label trial in ASD in 2019. An investigator-led 100 patient placebo-controlled trial in ASD also commenced in 2019. An investigator-led open label study of CBDV in children with Rett syndrome and seizures is ongoing. CBDV in Rett syndrome has received Orphan Drug Designation from the FDA.

In February 2018, we announced that a Phase 2a study of CBDV in adult patients with focal seizures did not meet its primary endpoint and showed a favorable safety and tolerability profile. We are currently evaluating next steps for this indication.

We have a portfolio of intellectual property relating to CBDV for use in various indications including epilepsy and autism spectrum disorder. These patent families include issued and pending claims to use CBDV alone or in combination with standard anti-epileptic drugs in the treatment of seizures, and pending claims to the use of CBDV in the treatment of ASD and associated conditions. Other families include pending claims directed to the use of CBDV in other therapeutic areas such as neuropathic pain, Alzheimer's disease and Duchenne's disease, CBDV compositions and CBDV extracts. We anticipate additional patent applications being filed as new data is generated.

Intravenous GWP42003 (CBD) in Neonatal Hypoxic-Ischemic Encephalopathy (NHIE)

NHIE is acute or sub-acute brain injury due to asphyxia caused during birth resulting from deprivation of oxygen, referred to as hypoxia, as a result of a sentinel event such as ruptured placenta, parental shock and even increased heart rate. Hypoxic damage can occur to most of the infant's organs, but brain damage is the most serious and least likely to heal, resulting in encephalopathy. This can later manifest itself as either mental retardation (including developmental delay and/or intellectual disability) or physical disabilities such as spasticity, blindness and deafness. Spastic diplegia and the other manifestations of cerebral palsy often feature asphyxiation during the birth process as a contributing factor. The exact timing and underlying causes of these outcomes remains unknown, but it is widely stipulated that interventions need to be administered within six hours of the hypoxic insult.

According to Kurinczuk. et al. in the 2010 edition of *Early Human Development*, the incidence of NHIE is 1.5 to 2.8 per 1,000 births in the U.S., or, by our estimate, 6,500 to 12,000 cases per year. Of these, 35 percent are expected to die in early life and 30 percent of cases will result in permanent disability. There are currently no FDA-approved medicines specifically indicated for NHIE. The only FDA-approved treatment is the Olympic Cool-Cap System and treatment guidelines in many European countries also support use of whole-body hypothermia.

We held a pre-IND meeting with the FDA to discuss the development program for an intravenous CBD formulation in the treatment of NHIE. In April 2015, we received Orphan Drug Designation from the FDA for CBD for the treatment of NHIE and in July 2015 we received fast track designation. In July 2015 we received Orphan Drug Designation from the EMA for CBD for the treatment of perinatal asphyxia, an alternate term that describes the same condition. A Phase 1 trial of intravenous GWP42003 in healthy volunteers was completed, and we are now recruiting for a Phase 2 trial in neonates.

Our portfolio of intellectual property related to the use of cannabinoids in NHIE includes a number of issued patents and pending applications in both the U.S. and Europe. This portfolio is directed to the use of cannabidiol in the treatment of NHIE and product formulations.

Business Strategy

Our goal is to capitalize on our leading position in the field of plant-derived cannabinoid therapeutics by pursuing the following strategies:

- Commercialize our lead product candidate Epidiolex in Dravet syndrome and LGS in the U.S. and Europe using our own commercial organization, and to identify the optimal commercial pathway in other markets around the world.
- Expand the market opportunity for Epidiolex within the field of epilepsy through the approval of the TSC indication, and expand beyond seizure indications initially by targeting the treatment of Rett syndrome.
- Seek U.S. approval for nabiximols in the treatment of MS spasticity, commercialize nabiximols in the U.S. using our own commercial organization, and expand the market to new indications.

- Advance several clinical-stage proprietary cannabinoid product candidates to late-stage development.
- Leverage our proprietary cannabinoid product platform and world leading position to discover, develop and commercialize additional novel first-in-class cannabinoid products.
- Further strengthen our lead competitive position.

Our Proprietary Cannabinoid Product Platform

We believe we have established a world-leading position in cannabinoid therapeutics through our proven proprietary cannabinoid product platform. Our platform consists of a continually evolving library of internally generated novel cannabis plant types that produce selected cannabinoids, discovery of novel cannabinoid pharmacology through our network of world leading scientists, a global intellectual property portfolio, in-house formulation, processing and manufacturing capabilities, and development and regulatory expertise. We further believe that we are in a unique position to develop and manufacture plant-derived cannabinoid formulations worldwide at sufficient quality, uniformity, scale and sophistication for the purposes of pharmaceutical development and to meet international regulatory requirements.

Cannabinoid Science Overview

Although one cannabinoid, THC, is known to cause specific euphoric effects, no other cannabinoid is known to share these properties. In recent decades, there have been major scientific advances that have led to the discovery of new plant-derived cannabinoids and the endocannabinoid system. We believe we are at the forefront of this science and our research into a large number of these cannabinoids suggests that each has distinct pharmacological effects. Although more studies are required to establish the clinical significance of these effects, they clearly have the potential to have therapeutic applications.

Our research to date has focused on the following plant-based cannabinoids:

CBD (Cannabidiol)
CBDV (Cannabidivarin)
CBDA (Cannabidiol — Acid)
CBDVA (Cannabidivarin — Acid)
CBC (Cannabichromene)
CBG (Cannabigerol)
CBGA (Cannabigerol — Acid)
CBGV (Cannabigerovarin)
CBN (Cannabinol)
CBNV (Cannabinovarin)
D8-THC (Delta-8 Tetrahydrocannabinol)
THC (Delta-9 Tetrahydrocannabinol)
THCA (Tetrahydrocannabinol — Acid)
THCV (Tetrahydrocannabivarin)
THCVA (Tetrahydrocannabivarin — Acid)

There are at least two types of cannabinoid receptors, CB1 and CB2, in the human endocannabinoid system. CB1 receptors are considered to be among the most widely expressed G protein-coupled receptors in the brain and are particularly abundant in areas of the brain concerned with movement and postural control, pain and sensory perception, memory, cognition, emotion, and autonomic and endocrine function. CB1 receptors are also found in peripheral tissues including peripheral nerves and non-neuronal tissues such as muscle, liver tissues and fat. CB2 receptors are expressed primarily in tissues in the immune system and are believed to mediate the immunological effects of cannabinoids. In addition, research suggests that beyond this endocannabinoid system non-THC cannabinoids interact with other important neurotransmitter and neuromodulatory systems in the human body, including G-protein coupled receptors, transient receptor potential channels, adenosine uptake and serotonin receptors. The far-reaching and diverse pharmacology of the numerous cannabinoids provides significant potential for development of cannabinoid therapeutics across many indications and disease areas.

Our Product Development Approach

Our approach to early product development of novel cannabinoids consists of the following stages:

Cannabinoid Chemotype Development. Our research activities commence with the generation of novel and proprietary cannabinoid plant types that produce selected cannabinoids. Our plant geneticists breed unique and protected chemotypes, or plants characterized by their chemical content, such that we can precisely control the cannabinoid composition of a plant. We employ traditional and molecular methods of plant breeding, with no use of genetic modification. We select chemotypes on the basis of their cannabinoid profile, appropriate levels of ingredients and botanical characteristics that enable commercial viability.

Active Pharmaceutical Ingredient Preparation. After we generate the unique chemotypes, we develop and characterize preparations from an extract of the chemotype. In addition to preparing whole plant extracts, we also modify the extract preparations by adding or removing certain components or purifying preparations to produce a purified cannabinoid. Each of these steps may give rise to patentable inventions.

Pharmacologic Evaluation. We then conduct *in vitro* and *in vivo* pharmacologic evaluation studies in validated disease models, testing the potential activity, safety and routes of drug metabolism of each cannabinoid preparation as well as combinations of preparations. These studies seek to identify the pharmacology of cannabinoid preparations and allow us to determine the potential therapeutic area in which they might have promise. We then conduct additional pharmacology, toxicology and pre-clinical development on promising preparations.

We conduct most of our pharmacologic evaluations in collaboration with cannabinoid scientists at academic institutions around the world. We enter into research collaboration agreements and other arrangements that enable us to benefit from the expertise of external scientists while retaining intellectual property rights that emerge from the study of our research materials.

Product Composition and Formulation Development. In parallel with the later stages of pharmacological evaluation, we identify optimum extraction and processing methods for the most promising preparations and then develop clinical formulations from the plant extract and analytical methodologies to further study the formulations. We are able to develop formulations of potential product candidates that focus on one or more cannabinoids as key active constituents, those that harness the complexity of the whole plant extract, as well as formulations that focus on a single cannabinoid. Each of these steps may give rise to patentable inventions.

With respect to complex extracts, our formulation approach is exemplified by nabiximols, the first approved cannabinoid therapeutic based on whole plant extracts from the cannabis plant. The main active ingredients of nabiximols, THC and CBD, are extracted from two proprietary chemotypes. In addition to THC and CBD, nabiximols contains additional cannabinoid and non-cannabinoid plant components. In order to achieve a fully standardized formulation of these complex extracts, we employ a range of advanced analytical technologies to demonstrate batch-to-batch uniformity. We standardize the formulation across the extract as a whole, not simply by reference to their key active components.

With respect to pure cannabinoid formulations, our approach is exemplified by Epidiolex. The active ingredient, CBD, is extracted from proprietary CBD containing chemotypes and then undergoes various processing steps to generate the isolated highly-purified compound.

Clinical development. Selected cannabinoid product candidates progress into clinical development. We have an in-house clinical operations team that has the proven capability to execute Phase 1, 2, 3 and 4 trials rapidly and cost effectively, and to support regulatory approvals. Since our inception, we have undertaken an extensive program of clinical trials.

Manufacturing

We are responsible for the manufacture and supply of our products for commercial and clinical purposes. Some of these manufacturing activities are contracted to external third parties.

Good Manufacturing Practices, or GMP, manufacturing licenses issued by the Medicines and Healthcare products Regulatory Agency, or MHRA, in the U.K. and our facilities have been audited by the MHRA, the FDA, and other international agencies. We have extensive in-house experience in production of botanical raw material, pharmaceutical production, quality control, quality assurance and supply chain management.

We have successfully exported cannabinoid commercial or research materials to more than 30 countries and have the necessary in-house expertise to manage the import/export process worldwide. For Epidiolex, our supply chain partners have obtained the permits and licenses necessary to support importation into the U.S. We have substantial expertise in, and experience with, relevant international, U.S. federal, and U.S. state regulations in relation to the research, distribution and commercialization of cannabinoid therapeutics. We have formed relationships with relevant international, U.S. federal, and U.S. state agencies in order to enable licensing of research sites, establishing appropriate product distribution channels and securing licensed storage, obtaining import/export licenses, and facilitating amendments to relevant legislation if required for commercialization.

Intellectual Property

Our success depends in significant part on our ability to protect the proprietary elements of Epidiolex, nabiximols and our other product candidates, technology and know-how, to operate without infringing on the proprietary rights of others, and to defend challenges and oppositions from others and prevent others from infringing on our proprietary rights. We have sought, and will continue to seek, patent protection in the U.S. and other countries for our proprietary technologies. Our intellectual property portfolio includes 85 patent families with issued and/or pending claims directed to plants, plant extracts, extraction technology, pharmaceutical formulations, drug delivery and the therapeutic uses of cannabinoids, as well as plant variety rights, know-how and trade secrets. From

these families, as of January 31, 2020, we own and/or license 259 pending patent applications worldwide. Within the U.S., we have 57 issued patents with a further 40 pending patent applications under active prosecution. There are an additional 767 issued patents outside of the U.S. Our policy is to seek patent protection for the technology, inventions and improvements that we consider important to the development of our business, but only in those cases where we believe that the costs of obtaining patent protection is justified by the commercial potential of the technology, and typically only in those jurisdictions that we believe present significant commercial opportunities.

We also rely on trademarks, trade secrets, know-how and continuing innovation to develop and maintain our competitive position.

Our strategy is to seek and obtain patents related to our products across all major pharmaceutical markets around the world. We have a portfolio of intellectual property relating to the use of CBD in various conditions, including epilepsy and schizophrenia; and the use of CBDV in various conditions, including ASD and epilepsy. We also hold several patent families covering nabiximols. We anticipate additional patent applications being filed as new data is generated.

Under the 2007 research collaboration agreement with Otsuka Pharmaceutical Co., Ltd., or Otsuka, which expired in June 2013, all intellectual property (including both patents and non-manufacturing related know-how) that was conceived by either Otsuka or us during the course of the collaboration is jointly owned by Otsuka and us. We have an exclusive sub-licensable royalty-bearing license to it both outside and within the fields of CNS and oncology.

The term of individual patents depends upon the countries in which they are obtained. In most countries in which we have filed, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the U.S., a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in granting a patent, or may be shortened if a patent is terminally disclaimed over another patent.

The term of a patent that covers an FDA-approved drug may also be eligible for extension, which permits term restoration as compensation for the term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits an extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Extensions cannot extend the remaining term of a patent beyond 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions to extend the term of a patent that covers an approved drug are available in Europe and other non-U.S. jurisdictions; indeed, Supplementary Protection Certificates have been applied for such that the European formulation patent for nabiximols will be extended to 2025 in Europe. We may apply for extensions on patents covering FDA approval of Epidiolex.

To protect our rights to any of our issued patents and proprietary information, we may need to litigate against infringing third parties, avail ourselves of the courts or participate in hearings to determine the scope and validity of those patents or other proprietary rights.

We also rely on trade secret protection for our confidential and proprietary information, and it is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us.

From time to time, in the normal course of our operations, we will be a party to litigation and other dispute matters and claims relating to intellectual property. One of our European patents is currently the subject of appeal proceedings following successfully overcoming the opposition filed against it. Such proceedings may result in claims in these patents being narrowed or cancelled such that the scope of the patent may not be as broad, or the patent may be revoked in its entirety. Our U.S. patent claiming the use of CBD in the treatment of partial seizures is also subject of a petition for *inter partes* review by the Patents Trial and Appeal Board of the USPTO. A hearing was held in April 2018 and a final decision was issued in January 2019. Claims 1 and 2 of the patent were invalidated and the remaining claims remain. An interference action was commenced in January 2019 against our U.S. patent claiming the use of a 1:1 ratio CBD:THC in the treatment of glioblastoma multiforme. A final decision in this matter is not expected until late 2020/early 2021. Litigation can be expensive and disruptive to normal business operations. Moreover, the results of complex legal proceedings are difficult to predict and our view of these matters may change in the future as the litigation and events related thereto unfold. An unfavorable outcome to any legal matter, if material, could have a materially adverse effect on our operations or our financial position, liquidity or results of operations.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our scientific knowledge, technology and development experience provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We are aware of exploratory research into the effects of THC and CBD drug formulations. We are aware of discovery research within the pharmaceutical industry into synthetic agonists and antagonists of CB1 and CB2 receptors. We are also aware of companies that supply synthetic cannabinoids and cannabis extracts to researchers for pre-clinical and clinical investigation. We are also aware of various companies that cultivate cannabis plants with a view to supplying herbal cannabis or nonpharmaceutical cannabis-based formulations to patients. These activities have not been approved by the FDA.

Patients in the U.S. suffering from seizures associated with Dravet or LGS are treated with a variety of FDA-approved products, including cannabidiol, clobazam, clonazepam, valproate, lamotrigine, levetiracetam, rufinamide, topiramate, ethosuximide, and zonisamide. Zogenix, Inc. submitted their NDA for low-dose fenfluramine, or Fintepla, in Dravet syndrome in September 2019. Ovid Therapeutics Inc./Takeda Pharmaceutical Company Limited and Marinus Pharmaceuticals, Inc. are developing therapies for treating Developmental and Epileptic Encephalopathies (includes Dravet and LGS). Stiripentol has been approved in Europe for several years to treat Dravet syndrome and was approved in 2018 by the FDA. Zynerba Pharmaceuticals, Inc. is developing a topical formulation of CBD, for which it has completed enrollment in its pivotal trial in Fragile X syndrome.

In MS spasticity, nabiximols aims to treat patients who do not respond adequately to standard care. In MS spasticity, such treatments include baclofen and tizanidine.

With respect to CBD, a number of nonapproved and nonstandardized artisanal, vernacular CBD preparations derived from crude herbal cannabis have been made available in limited quantities by producers of “medical marijuana” in the U.S. We have never endorsed or supported the idea of distributing or legalizing crude herbal cannabis, or preparations derived from crude herbal cannabis for medical use and do not believe prescription cannabinoids are the same, and therefore competitive with, crude herbal cannabis. We have consistently maintained that only a cannabinoid medication, one that is standardized in composition, formulation and dose, administered by means of an appropriate delivery system, and tested in properly controlled pre-clinical and clinical studies, can meet the standards of regulatory authorities around the world, including those of the FDA. We have also repeatedly stressed that these regulatory processes provide important protections for patients, and we believe that any cannabinoid medication must be subjected to, and satisfy, such rigorous scrutiny.

Government Regulation and Product Approvals

FDA Approval Process

In the U.S., pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as imposition of clinical holds, FDA refusal to approve pending NDAs, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, civil penalties and criminal prosecution.

Pharmaceutical product development in the U.S. typically involves pre-clinical laboratory and animal tests and the submission to the FDA of an IND, which must become effective before clinical testing may commence. For commercial approval, the sponsor must submit adequate tests by all methods reasonably applicable to show that the drug is safe for use under the conditions prescribed, recommended or suggested in the proposed labeling. The sponsor must also submit substantial evidence, generally consisting of adequate, well-controlled clinical trials to establish that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended or suggested in the proposed labeling. In certain cases, the FDA may determine that a drug is effective based on one clinical study plus confirmatory evidence. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Pre-clinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the pre-clinical tests must comply with federal regulations and requirements, including the FDA’s good laboratory practices regulations and the U.S. Department of Agriculture’s, or USDA’s, regulations implementing the Animal Welfare Act. The results of pre-clinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term pre-clinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has not imposed a clinical hold on the IND or otherwise commented or questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations, (ii) in compliance with GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors, and (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The trial protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In general in Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication, dosage tolerance and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. The FDA may, however, determine that a drug is effective based on one clinical study plus confirmatory evidence. Only a small percentage of investigational drugs complete all three phases and obtain marketing approval. In some cases, the FDA may require post-market studies, known as Phase 4 studies, to be conducted as a condition of approval in order to gather additional information on the drug's effect in various populations and any side effects associated with long-term use. Depending on the risks posed by the drugs, other post-market requirements may be imposed.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. The FDA approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all pre-clinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA is substantial.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. Under the statute and implementing regulations, the FDA has 180 days (the initial review cycle) from the date of filing to issue either an approval letter or a complete response letter, unless the review period is adjusted by mutual agreement between the FDA and the applicant or as a result of the applicant submitting a major amendment. In practice, the performance goals established pursuant to the Prescription Drug User Fee Act have effectively extended the initial review cycle beyond 180 days. The FDA's current performance goals call for the FDA to complete review of 90 percent of standard (non-priority) NDAs within 10 months of receipt and within six months for priority NDAs, but two additional months are added to standard and priority NDAs for a new molecular entity, or NME.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an advisory committee, which is typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the product unless compliance with current GMP is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing 90 percent of resubmissions within two to six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for health care professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of certain FDA-regulated products, including prescription drugs, are required to register and disclose certain clinical trial information on a public website maintained by the U.S. National Institutes of Health. Information related to the product, patient population, phase of investigation, study sites and investigator, and other aspects of the clinical trial is made public as part of the registration. Under a new rule, effective January 18, 2017, sponsors are also obligated to disclose the results of these trials after completion. Disclosure of the results of these trials can be delayed for up to two years if the sponsor certifies that it is seeking approval of an unapproved product or that it will file an application for approval of a new indication for an approved product within one year. Competitors may use this publicly available information to gain knowledge regarding the design and progress of our development programs.

Fast Track Designation and Accelerated Approval

The FDA is required to facilitate the development, and expedite the review, of drugs that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the Fast Track Program, the sponsor of a new drug candidate may request that the FDA designate the drug candidate for a specific indication as a Fast Track drug concurrent with, or after, the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for Fast Track designation within 60 days of receipt of the sponsor's request.

Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. Unless otherwise informed by the FDA, for an accelerated approval product an applicant must submit to the FDA for consideration during the preapproval review period copies of all promotional materials, including promotional labeling as well as advertisements, intended for dissemination or publication within 120 days following marketing approval. After 120 days following marketing approval, unless otherwise informed by the FDA, the applicant must submit promotional materials at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement

In addition to other benefits such as the ability to use surrogate endpoints and engage in more frequent interactions with the FDA, the FDA may initiate review of sections of a Fast Track drug's NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. Additionally, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

The Hatch-Waxman Act

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be bioequivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, pre-clinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are considered to be therapeutically equivalent to the listed drug, are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug in accordance with state law.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement, certifying that its proposed ANDA labeling does not contain (or carve out) any language regarding the patented method-of-use, rather than certify to a listed method-of-use patent.

If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Exclusivity

Upon NDA approval of a new chemical entity or NCE, which is a drug that contains no active moiety that has been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which time the FDA cannot receive any ANDA or 505(b)(2) application seeking approval of a drug that references a version of the NCE drug. Certain changes to a drug, such as the addition of a new indication to the package insert, are associated with a three-year period of exclusivity during which the FDA cannot approve an ANDA or 505(b)(2) application that includes the change.

An ANDA or 505(b)(2) application may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification and thus no ANDA or 505(b)(2) application may be filed before the expiration of the exclusivity period.

For a botanical drug, the FDA may determine that the active moiety is one or more of the principal components or the complex mixture as a whole. This determination would affect the utility of any five-year exclusivity as well as the ability of any potential generic competitor to demonstrate that it is the same drug as the original botanical drug.

Five-year and three-year exclusivities do not preclude FDA approval of a 505(b)(1) application for a duplicate version of the drug during the period of exclusivity, provided that the 505(b)(1) applicant conducts or obtains a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Patent Term Extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent extension. The allowable patent term extension is calculated as half of the drug's testing phase — the time between IND submission and NDA submission — and all of the review phase — the time between NDA submission and approval up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years.

For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the USPTO must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition — generally a disease or condition that affects fewer than 200,000 individuals in the U.S (or affects more than 200,000 in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for such disease or condition will be recovered from sales in the U.S. of such drug). Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the U.S. for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. If the FDA designates an orphan drug based on a finding of clinical superiority, the FDA must provide a written notification to the sponsor that states the basis for orphan designation, including “any plausible hypothesis” relied upon by the FDA. The FDA must also publish a summary of its clinical superiority findings upon granting orphan drug exclusivity based on clinical superiority. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

Special Protocol Assessment

A company may reach an agreement with the FDA under the Special Protocol Assessment, or SPA, process as to the required design and size of clinical trials intended to form the primary basis of an efficacy claim. According to its performance goals, the FDA is supposed to evaluate the protocol within 45 days of the request to assess whether the proposed trial is adequate, and that evaluation may result in discussions and a request for additional information. A SPA request must be made before the proposed trial begins, and all open issues must be resolved before the trial begins. If a written agreement is reached, it will be documented and made part of the administrative record. Under the FDC Act and FDA guidance implementing the statutory requirement, an SPA is generally binding upon the FDA except in limited circumstances, such as if the FDA identifies a substantial scientific issue essential to determining safety or efficacy after the study begins, public health concerns emerge that were unrecognized at the time of the protocol assessment, the sponsor and the FDA agree to the change in writing, or if the study sponsor fails to follow the protocol that was agreed upon with the FDA.

Advertising and Promotion

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs.

Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Adverse Event Reporting and GMP Compliance

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, may require under a REMS special communication regarding the safety of the drug or heightened surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality-control, drug manufacture, packaging, and labeling procedures must continue to conform to GMP, after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with GMP. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with GMP. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing or if previously unrecognized problems are subsequently discovered.

Pediatric Exclusivity and Pediatric Use

The Best Pharmaceuticals for Children Act, or BPCA, provides NDA holders a six-month period of exclusivity attached to any other exclusivity listed with the FDA — patent or non-patent — for a drug if certain conditions are met. Conditions for pediatric exclusivity include a determination by the FDA that information relating to the use of a new drug in the pediatric population may produce health benefits in that population; a written request by the FDA for pediatric studies; and agreement by the applicant to perform the requested studies and the submission to the FDA, completion of the studies in accordance with the written request, and the acceptance by the FDA, of the reports of the requested studies within the statutory time frame. Applications under the BPCA are treated as priority applications.

In addition, under the Pediatric Research Equity Act, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective, unless the sponsor has received a deferral or waiver from the FDA. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted. The sponsor or the FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data need to be collected before the pediatric studies begin. Under PREA, the FDA must send a noncompliance letter requesting a response within 45 days to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Controlled Substances

The federal Controlled Substances Act of 1970, or CSA, and its implementing regulations establish a “closed system” of regulations for controlled substances. The CSA imposes registration, security, recordkeeping and reporting, storage, manufacturing, distribution, importation and other requirements under the oversight of the DEA. The DEA is the federal agency responsible for regulating controlled substances, and requires those individuals or entities that manufacture, import, export, distribute, research, or dispense controlled substances to comply with the regulatory requirements in order to prevent the diversion of controlled substances to illicit channels of commerce.

The DEA categorizes controlled substances into one of five schedules — Schedule I, II, III, IV or V — with varying qualifications for listing in each schedule. Schedule I substances by definition have a high potential for abuse, have no currently accepted medical use in treatment in the U.S. and lack accepted safety for use under medical supervision. Pharmaceutical products having a currently accepted medical use that are otherwise approved for marketing may be listed as Schedule II, III, IV or V substances, with Schedule II substances presenting the highest potential for abuse and physical or psychological dependence, and Schedule V substances presenting the lowest relative potential for abuse and dependence. Epidiolex is a Schedule V controlled substance. Nabiximols, if approved in the U.S., will require scheduling by the DEA before it can be marketed.

Facilities that manufacture, distribute, import or export any controlled substance must register annually with the DEA. The DEA registration is specific to the particular location, activity(ies) and controlled substance schedule(s). For example, separate registrations are required for importation and manufacturing activities, and each registration authorizes which schedules of controlled substances the registrant may handle. However, certain coincident activities are permitted without obtaining a separate DEA registration, such as distribution of controlled substances by the manufacturer that produces them.

The DEA inspects all manufacturing facilities to review security, recordkeeping, reporting and handling prior to issuing a controlled substance registration. The specific security requirements vary by the type of business activity and the schedule and quantity of controlled substances handled. The most stringent requirements apply to manufacturers of Schedule I and Schedule II substances. Required security measures commonly include background checks on employees and physical control of controlled substances through storage in approved vaults, safes and cages, and through use of alarm systems and surveillance cameras. An application for a manufacturing registration as a bulk manufacturer (not a dosage form manufacturer or a repacker/relabeler) for a Schedule I or II substance must be published in the Federal Register, and is open for 60 days to permit interested persons to submit comments, objections or requests for a hearing. A copy of the notice of the Federal Register publication is simultaneously forwarded by DEA to all those registered, or applicants for registration, as bulk manufacturers of that substance. Once registered, manufacturing facilities must maintain records documenting the manufacture, receipt and distribution of all controlled substances. Manufacturers must submit periodic reports to the DEA of the distribution of Schedule I and II controlled substances, Schedule III narcotic substances, and other designated substances. Registrants must also report any controlled substance thefts or significant losses, and must obtain authorization to destroy or dispose of controlled substances. As with applications for registration as a bulk manufacturer, an application for an importer registration for a Schedule I or II substance must also be published in the Federal Register, which remains open for 30 days for comments. Imports of Schedule I and II controlled substances for commercial purposes are generally restricted to substances not already available from a domestic supplier or where there is not adequate competition among domestic suppliers. In addition to an importer or exporter registration, importers and exporters must obtain a permit for every import or export of a Schedule I and II substance or Schedule III, IV and V narcotic, and submit import or export declarations for Schedule III, IV and V non-narcotics. In some cases, Schedule III non-narcotic substances may be subject to the import/export permit requirement, if necessary to ensure that the U.S. complies with its obligations under international drug control treaties.

For drugs manufactured in the U.S., the DEA establishes annually an aggregate quota for the amount of substances within Schedules I and II that may be manufactured or produced in the U.S. based on the DEA's estimate of the quantity needed to meet legitimate medical, scientific, research and industrial needs. This limited aggregate amount of cannabis that the DEA allows to be produced in the U.S. each year is allocated among individual companies, which, in turn, must annually apply to the DEA for individual manufacturing and procurement quotas. The quotas apply equally to the manufacturing of the active pharmaceutical ingredient and production of dosage forms. The DEA may adjust aggregate production quotas a few times per year, and individual manufacturing or procurement quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make such adjustments for individual companies.

The states also maintain separate controlled substance laws and regulations, including licensing, recordkeeping, security, distribution, and dispensing requirements. State Authorities, including Boards of Pharmacy, regulate use of controlled substances in each state. Failure to maintain compliance with applicable requirements, particularly as manifested in the loss or diversion of controlled substances, can result in enforcement action that could have a material adverse effect on our business, operations and financial condition. The DEA may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to revoke those registrations. In certain circumstances, violations could lead to criminal prosecution.

Europe/Rest of World Government Regulation

In addition to regulations in the U.S., we are and will be subject, either directly or through our distribution partners, to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales (including pricing and reimbursement) and distribution of our products, if approved.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in non-U.S. countries prior to the commencement of clinical trials or marketing of the product in those countries.

In the European Union, medicinal products are subject to extensive pre- and post-marketing regulation by regulatory authorities at both the European Union and national levels. Additional rules also apply at the national level to the manufacture, import, export, storage, distribution and sale of controlled substances. In many European Union member states the regulatory authority responsible for medicinal products is also responsible for controlled substances. Responsibility is, however, split in some member states, such as the U.K. Generally, any company manufacturing or distributing a medicinal product containing a controlled substance in the European Union will need to hold a controlled substances license from the competent national authority and will be subject to specific record-keeping and security obligations. Separate import or export certificates are required for each shipment into or out of the member state.

Clinical Trials and Marketing Approval

Certain countries outside of the U.S. have a process that requires the submission of a clinical trial application much like an IND prior to the commencement of human clinical trials. In Europe, for example, a clinical trial application, or CTA, must be submitted to the competent national health authority and to independent ethics committees in each country in which a company intends to conduct clinical trials. Once the CTA is approved in accordance with a country's requirements and a company has received favorable ethics committee approval, clinical trial development may proceed in that country.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country, even though there is already some degree of legal harmonization in the European Union member states resulting from the national implementation of underlying European Union legislation. In all cases, the clinical trials must be conducted in accordance with the International Conference on Harmonization, or ICH, guidelines on GCP and other applicable regulatory requirements.

To obtain regulatory approval to place a drug on the market in European Union countries, we must submit a marketing authorization application. This application is similar to the NDA in the U.S., with the exception of, among other things, country-specific document requirements. All application procedures require an application in the common technical document, or CTD, format, which includes the submission of detailed information about the manufacturing and quality of the product, and nonclinical and clinical trial information. Drugs can be authorized in the European Union by using (i) the centralized authorization procedure, (ii) the mutual recognition procedure, (iii) the decentralized procedure or (iv) national authorization procedures. The initial Sativex approvals were a consequence of an application under the De-Centralized Procedure, or DCP, to the E.U. member states of the U.K. and Spain.

The European Commission created the centralized procedure for the approval of human drugs to facilitate marketing authorizations that are valid throughout the European Union and, by extension (after national implementing decisions) in Iceland, Liechtenstein and Norway, which, together with the European Union member states, comprise the European Economic Area, or EEA. Applicants file marketing authorization applications with the European Medicines Agency, or EMA, where they are reviewed by a relevant scientific committee, in most cases the Committee for Medicinal Products for Human Use, or CHMP. The EMA forwards

CHMP opinions to the European Commission, which uses them as the basis for deciding whether to grant a marketing authorization. This procedure results in a single marketing authorization granted by the European Commission that is valid across the European Union, as well as in Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for human drugs that are: (i) derived from biotechnology processes, such as genetic engineering, (ii) contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions and viral diseases, (iii) officially designated "orphan drugs" (drugs used for rare human diseases) and (iv) advanced-therapy medicines, such as gene-therapy, somatic cell-therapy or tissue-engineered medicines. The centralized procedure may at the voluntary request of the applicant also be used for human drugs that do not fall within the above-mentioned categories if the CHMP agrees that the human drug (a) contains a new active substance not yet approved on November 20, 2005; (b) constitutes a significant therapeutic, scientific or technical innovation or (c) authorization under the centralized procedure is in the interests of patients at the European Union level.

Under the centralized procedure in the European Union, the maximum time frame for the evaluation of a marketing authorization application by the EMA is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP), with adoption of the actual marketing authorization by the European Commission thereafter.

Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest from the point of view of therapeutic innovation, defined by three cumulative criteria: the seriousness of the disease to be treated; the absence of an appropriate alternative therapeutic approach, and anticipation of exceptional high therapeutic benefit. In this circumstance, EMA ensures that the evaluation for the opinion of the CHMP is completed within 150 days and the opinion issued thereafter.

For those medicinal products for which the centralized procedure is not available, the applicant must submit marketing authorization applications to the national medicines regulators through one of three procedures: (i) the mutual recognition procedure (which must be used if the product has already been authorized in at least one other European Union member state, and in which the European Union member states are required to grant an authorization recognizing the existing authorization in the other European Union member state, unless they identify a serious risk to public health), (ii) the decentralized procedure (in which applications are submitted simultaneously in two or more European Union member states) or (iii) national authorization procedures (which results in a marketing authorization in a single European Union member state).

Mutual Recognition Procedure

The mutual recognition procedure, or MRP, for the approval of human drugs is an alternative approach to facilitate individual national marketing authorizations within the European Union. Basically, the MRP may be applied for all human drugs for which the centralized procedure is not obligatory. The MRP is applicable to the majority of conventional medicinal products and must be used if the product has already been authorized in one or more member states. Since the first approvals for Sativex were national approvals in the U.K. and Spain (following a DCP), the only route open to us for additional marketing authorizations in the European Union was the MRP.

The characteristic of the MRP is that the procedure builds on an already-existing marketing authorization in a member state of the European Union that is used as a reference in order to obtain marketing authorizations in other European Union member states. In the MRP, a marketing authorization for a drug already exists in one or more member states of the European Union and subsequently marketing authorization applications are made in other European Union member states by referring to the initial marketing authorization. The member state in which the marketing authorization was first granted will then act as the reference member state. The member states where the marketing authorization is subsequently applied for act as concerned member states. The concerned member states are required to grant an authorization recognizing the existing authorization in the reference member state, unless they identify a serious risk to public health.

The MRP is based on the principle of the mutual recognition by European Union member states of their respective national marketing authorizations. Based on a marketing authorization in the reference member state, the applicant may apply for marketing authorizations in other member states. In such case, the reference member state shall update its existing assessment report about the drug in 90 days. After the assessment is completed, copies of the report are sent to all member states, together with the approved summary of product characteristics, labeling and package leaflet. The concerned member states then have 90 days to recognize the decision of the reference member state and the summary of product characteristics, labeling and package leaflet. National marketing authorizations shall be granted within 30 days after acknowledgement of the agreement.

Should any Member State refuse to recognize the marketing authorization by the reference member state, on the grounds of potential serious risk to public health, the issue will be referred to a coordination group. Within a time frame of 60 days, member states shall, within the coordination group, make all efforts to reach a consensus. If this fails, the procedure is submitted to an EMA scientific committee for arbitration. The opinion of this EMA Committee is then forwarded to the European Commission, for the start of the decision-making process. As in the centralized procedure, this process entails consulting various European Commission Directorates General and the Standing Committee on Human Medicinal Products. Since the initial approvals of Sativex in the U.K. and Spain, there have been three "waves" of additional approvals under three separate MRPs. Each of these procedures have been completed without any referral, and therefore without any delay.

Data Exclusivity

In the European Union, marketing authorization applications for generic medicinal products do not need to include the results of pre-clinical and clinical trials, but instead can refer to the data included in the marketing authorization of a reference product for which regulatory data exclusivity has expired. If a marketing authorization is granted for a medicinal product containing a new active substance, that product benefits from eight years of data exclusivity, during which generic marketing authorization applications referring to the data of that product may not be accepted by the regulatory authorities, and a further two years of market exclusivity, during which such generic products may not be placed on the market. The two-year period may be extended to three years if during the first eight years a new therapeutic indication with significant clinical benefit over existing therapies is approved.

Orphan Medicinal Products

The EMA's Committee for Orphan Medicinal Products, or COMP, may recommend orphan medicinal product designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the product in the European Union would be sufficient to justify the necessary investment in developing the medicinal product. The COMP may only recommend orphan medicinal product designation when the product in question offers a significant clinical benefit over existing approved products for the relevant indication. Following a positive opinion by the COMP, the European Commission adopts a decision granting orphan status. The COMP will reassess orphan status in parallel with EMA review of a marketing authorization application and orphan status may be withdrawn at that stage if it no longer fulfills the orphan criteria (for instance because in the meantime a new product was approved for the indication and no convincing data are available to demonstrate a significant benefit over that product). Orphan medicinal product designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following marketing authorization. During this period, the competent authorities may not accept or approve any similar medicinal product, unless it offers a significant clinical benefit. This period may be reduced to six years if the orphan medicinal product designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Pediatric Development

In the European Union, companies developing a new medicinal product must agree to a Pediatric Investigation Plan, or PIP, with the EMA and must conduct pediatric clinical trials in accordance with that PIP unless a waiver applies, for example, because the relevant disease or condition occurs only in adults. The marketing authorization application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted, in which case the pediatric clinical trials must be completed at a later date. Products that are granted a marketing authorization on the basis of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six-month extension of the protection under a supplementary protection certificate (if the product covered by it qualifies for one at the time of approval). This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

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

In addition, most countries are parties to the Single Convention on Narcotic Drugs 1961, which governs international trade and domestic control of narcotic substances, including cannabis extracts. Countries may interpret and implement their treaty obligations in a way that creates a legal obstacle to our obtaining marketing approval for Sativex and our other products in those countries. These countries may not be willing or able to amend or otherwise modify their laws and regulations to permit Sativex or our other products to be marketed or achieving such amendments to the laws and regulations may take a prolonged period of time. In that case, we would be unable to market our products in those countries in the near future or perhaps at all.

Reimbursement

Sales of pharmaceutical products in the U.S. depend, in part, on the extent to which the costs of the products will be covered by third-party payers, such as government health programs, and commercial insurance and managed health care organizations. These third-party payers are increasingly challenging the prices charged for medical products and services. Additionally, the containment of health care costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, utilization management and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. If these third-party payers do not consider our products to be cost effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposed requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries and included a major expansion of the prescription drug benefit under Medicare Part D. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Part D is available through both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Parts A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from nongovernmental payers.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. This research is overseen by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures must be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payers, it is not clear how such a result could be avoided and what if any effect the research will have on the sales of our product candidates, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payer to not cover our product candidates could reduce physician usage of the product candidate and have a material adverse effect on our sales, results of operations and financial condition.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, the ACA) was enacted in March 2010. The ACA was enacted with the goal of expanding coverage for the uninsured while at the same time containing overall health care costs. With regard to pharmaceutical products, among other things, the ACA expanded and increased industry rebates for drugs covered under Medicaid programs and made changes to the coverage requirements under the Medicare D program. The ongoing legal challenges to the ACA, as well as Congressional efforts to repeal the ACA, create uncertainty as to the future impact of the ACA on pharmaceutical products.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, some European Union jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. Such differences in national pricing regimes may create price differentials between European Union member states. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the U.S. In the European Union, the downward pressure on healthcare costs in general, particularly prescription medicines, has become intense. As a result, barriers to entry of new products are becoming increasingly high and patients are unlikely to use a drug product that is not reimbursed by their government.

Other Health Care Laws and Compliance Requirements

In the U.S., our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services (formerly the Health Care Financing Administration), or CMS, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice and individual U.S. Attorney offices within the Department of Justice, and state and local governments. For example, sales, marketing and scientific/educational grant programs must comply with the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act, the privacy provisions of the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws, each as amended. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veterans Health Care Act of 1992, or VHCA, each as amended. If products are made available to authorized users of the Federal Supply Schedule, additional laws and requirements apply. Under the VHCA, drug companies are required to offer certain drugs at a reduced price to a number of federal agencies including the U.S. Department of Veteran Affairs and U.S. Department of Defense, the Public Health Service and certain private Public Health Service-designated entities in order to participate in other federal funding programs including Medicare and Medicaid. In addition, discounted prices must be offered for certain U.S. Department of Defense purchases for its TRICARE program via a rebate system. Participation under the VHCA requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers and distributors who ship products into the state, even if such manufacturers or distributors have no place of business within the state. Several states have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales and marketing activities or register their sales representatives. Other legislation has been enacted in certain states prohibiting certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

Legal Proceedings and Related Matters

From time to time, we may be a party to litigation that arises in the ordinary course of our business. We do not have any pending litigation that, separately or in the aggregate, would, in the opinion of management, have a material adverse effect on our results of operations, financial condition or cash flows.

Employees

The number of employees by function and geographic location as of the end of the period for our fiscal year ended December 31, 2019 was as follows:

	As of December 31, 2019
By Function:	
Research and development	278
Manufacturing and operations	192
Quality control and assurance	79
Commercial	198
Management and administrative	154
Total	901
By Geography:	
Switzerland	3
United Kingdom	604
North America	294
Total	901

We have never had a work stoppage and none of our employees are covered by collective bargaining agreements or represented by a labor union. We believe our relationships with our employees around the world are good.

Available Information

Access to our Annual Report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to these reports filed with or furnished to the SEC, may be obtained through the investor section of our website at http://www.gwpharm.com as soon as reasonably practical after we electronically file or furnish these reports. We do not charge for access to and viewing of these reports. Information in the investor section and on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated herein by reference. Our filings with the SEC may be accessed through the SEC's website at www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Financial Information

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

Corporate Information

Our registered and principal executive offices are located at Sovereign House, Vision Park, Chivers Way, Histon, Cambridge, CB24 9BZ, United Kingdom, our general telephone number is +44 1223 266 800 and our Internet address is *http://www.gwpharm.com.* Our website and the information contained on or accessible through our website are not part of this document.

Item 1A. Risk Factors

Our business has significant risks. You should carefully consider the following risk factors and all other information contained in this Annual Report, including our consolidated financial statements and the related notes. The risks and uncertainties described below are those significant risk factors currently known and specific to us that we believe are relevant to our business, results of operations and financial condition. Additional risks and uncertainties not currently known to us or that we now deem immaterial may also impair our business, results of operations and financial condition.

Risks Related to Our Business

Our prospects are highly dependent on the successful commercialization of Epidiolex/Epidyolex, which received approval in 2018 from the FDA and in September 2019 from the EC. To the extent Epidiolex/Epidyolex is not commercially successful, our business, financial condition and results of operations may be materially adversely affected and the price of our ADSs may decline.

Epidiolex is our only drug that has been approved for sale in the U.S., and it has been approved for sale in Europe. In the U.S., it has only been approved for the treatment of seizures associated with LGS and Dravet syndrome in patients two years of age and older. In Europe, Epidyolex has only been approved for use as adjunctive therapy of seizures associated with LGS or Dravet syndrome, in conjunction with clobazam, for patients two years of age and older. We are focusing a significant portion of our activities and resources on Epidiolex, and we believe our prospects are highly dependent on, and a significant portion of the value of our company relates to, our ability to successfully commercialize Epidiolex in the U.S. and Europe.

Successful commercialization of Epidiolex is subject to many risks. Prior to Epidiolex, we have only launched or commercialized one product, Sativex, outside of the U.S., and there is no guarantee that we will be able to continue to successfully commercialize Epidiolex for its approved indications. While we have established our commercial team and have hired our U.S. and European sales forces, we will need to continue to maintain and further develop the teams in order to successfully coordinate the commercialization of Epidiolex. Even if we are successful in maintaining and continuing to develop our commercial team, there are many factors that could cause the commercialization of Epidiolex to be unsuccessful, including a number of factors that are outside our control. Because no drug has previously been approved by the FDA for the treatment of seizures associated with Dravet syndrome prior to 2018, it is especially difficult to estimate the market potential of Epidiolex. The commercial success of Epidiolex depends on the extent to which patients and physicians accept and adopt Epidiolex as a treatment for LGS and Dravet syndrome, and we do not know whether our or others' estimates in this regard will be accurate. We have limited information about how physicians, patients and payers will respond to the pricing of Epidiolex. Physicians may not prescribe Epidiolex and patients may be unwilling to use Epidiolex if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, any negative development for Epidiolex in the market after launch, in clinical development for additional indications, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of Epidiolex. Thus, significant uncertainty remains regarding the commercial potential of Epidiolex.

If the launch or commercialization of Epidiolex is unsuccessful or perceived as disappointing, our share price could decline significantly and the long-term success of the product and the Company could be harmed.

If we do not obtain regulatory approval of Epidiolex for other indications in the U.S., Europe or for any indications in foreign jurisdictions, we will not be able to market Epidiolex for other indications or in other jurisdictions, which will limit our commercial revenues.

While Epidiolex has been approved by the FDA and EMA for the treatment of seizures associated with LGS and Dravet syndrome in patients two years of age and older, it has not been approved by the FDA or EMA for any other indications, and it has not been approved in any other jurisdiction for these indications or for any other indication. In order to market Epidiolex for other indications or in other jurisdictions, we must obtain regulatory approval for each of those indications and in each of the applicable jurisdictions, and we may never be able to obtain such approval. Approval of Epidiolex by the FDA and the EMA for the treatment of seizures associated with LGS and Dravet syndrome in patients two years of age and older does not ensure that the foreign jurisdictions will also approve Epidiolex for these indications, nor does it ensure that Epidiolex will be approved by the FDA for any other indication. The research, testing, manufacturing, labeling, approval, sale, import, export, marketing and distribution of pharmaceutical product candidates are subject to extensive regulation by the FDA and the EMA and other regulatory authorities in the U.S. and Europe and other countries, whose regulations differ from country to country. We will be required to comply with different regulations and policies of the jurisdictions where we seek approval for our product candidates, and, outside of the U.S. and Europe we have not yet identified all of the requirements that we will need to satisfy before submitting Epidiolex for approval for other indications or in other jurisdictions. In addition, some jurisdictions, including the U.S. and Europe, may impose further restrictions through designation of our products as controlled substances. This will require additional time, expertise and expense, including the potential need to conduct additional studies or development work for other jurisdictions beyond the work that we have conducted to support our NDA submission in LGS and Dravet syndrome. In addition, strategic considerations need to be taken into account when determining whether and when to submit Epidiolex for approval in other jurisdictions. If we do not receive marketing approval for Epidiolex for any other indication or from any regulatory agency other than the FDA and the EMA, we will never be able to commercialize Epidiolex for any other indication in the U.S. or Europe or for any indication in any other jurisdiction. Even if we do receive additional regulatory approvals, we may not be successful in commercializing those approved products.

If the results or timing of regulatory filings, the regulatory process, regulatory developments, clinical trials or nonclinical studies or other activities, actions or decisions related to Epidiolex do not meet our or others' expectations, the market price of our ADSs could decline significantly.

In 2018, we received FDA approval for Epidiolex for the treatment of seizures associated with LGS or Dravet syndrome in patients two years of age and older. In September 2019, we received EC approval of the marketing authorization for Epidyolex. Those approvals subject us to ongoing obligations and continued regulatory review, which may result in significant additional expense. If we do not meet those ongoing obligations, we could be subject to significant penalties, including market withdrawal and/or civil or criminal penalties. Additionally, our other product candidates, if approved, could be subject to labeling and other restrictions and we may be subject to penalties (including market withdrawal) if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

In 2018, we received FDA regulatory approval for Epidiolex for the treatment of seizures associated with LGS and Dravet syndrome in patients two years of age and older. In September 2019, we received EC approval of the marketing authorization for Epidyolex. We have received Orphan Drug Designation from the FDA for Epidiolex for seizures associated with LGS, Dravet syndrome and TSC. We also received Orphan Designation from the EMA's COMP for Epidyolex for Dravet syndrome, LGS and TSC, and the COMP reconfirmed the designation for LGS and Dravet syndrome upon the EC's approval. The FDA and EC's approvals and other regulatory approvals for any of our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase IV clinical trials, and surveillance to monitor the safety and efficacy of the approved product candidate. With respect to the FDA's and EMA's approvals of Epidiolex, we are subject to certain post-marketing requirements. Failure to comply with these post-marketing requirements could result in withdrawal of our marketing approval for Epidiolex and/or other civil or criminal penalties. In addition, with respect to Epidiolex, and any product candidate that the FDA, EMA or a comparable foreign regulatory authority approves, the manufacturing processes, labeling, packaging, distribution, import, export, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current Good Manufacturing Practices, or GMPs, with Good Clinical Practices, or GCPs, for any clinical trials that we conduct post-approval, and with Good Laboratory Practices, or GLPs, for any nonclinical studies.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, mandatory safety labeling changes or product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications submitted by us, or suspension or revocation of product approvals;
- imposition of risk evaluation and mitigation strategies, or REMS;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and EC's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of any of our product candidates or future indications for currently approved products. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we could lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Epidiolex has only been studied in a limited number of patients and in limited populations. As we continue our commercial launch, Epidiolex will become available to a much larger number of patients, and we do not know whether the results of Epidiolex use in such larger number of patients will be consistent with the results from our clinical trials.

Epidiolex has been administered only to a limited number of patients and in limited populations in clinical trials. While the FDA and EC granted approval of Epidiolex based on the data included in the NDA and marketing authorization application, and we believe such data to be robust, we do not know whether the results will be consistent with those resulting from administration of the drug to a large number of patients. New data relating to Epidiolex, including from adverse event reports and post-marketing studies in the U.S. and Europe, and from other ongoing clinical trials, may result in changes to the product label and/or imposition of a REMS and may adversely affect sales, or result in withdrawal of Epidiolex from the market. The FDA, EC and regulatory authorities in other jurisdictions may also consider the new data in reviewing Epidiolex marketing applications for indications other than our approved uses in other jurisdictions, or impose additional post-approval requirements. If any of these actions were to occur, it could result in significant expense and delay or limit our ability to generate sales revenues.

We are dependent on the success of our product candidates, some of which may not receive regulatory approval or be successfully commercialized.

Our success will depend on our ability to successfully commercialize our product pipeline, including commercialization of Epidiolex, nabiximols and our other cannabinoid product candidates. While we have received U.S. and EMA regulatory approval for the use of Epidiolex for the treatment of seizures associated with LGS or Dravet syndrome in patients two years of age and older, we are evaluating Epidiolex for the treatment of other conditions such as TSC. We also continue to develop Epidiolex for additional rare childhood-onset epilepsy disorders including Rett syndrome. Epidiolex may never receive regulatory approval for the treatment of any other indications in the U.S. or elsewhere. Even if completed Phase 3 clinical trials and/or ongoing or future Phase 3 clinical trials show positive results, there can be no assurance that the FDA, EMA or any other regulatory authority will approve Epidiolex for any additional indications or that any other product candidate will receive approval.

Our ability to successfully commercialize Epidiolex, nabiximols and our other product candidates will depend on, among other things, our ability to:

- successfully complete pre-clinical and other nonclinical studies and clinical trials, including assessment of abuse potential;
- demonstrate to the FDA, EMA and similar foreign regulatory authorities that the efficacy of Epidiolex, nabiximols or any other product candidates in clinical trials can be attributed to the investigative product and not exclusively to its interaction with concomitant medications. It is possible that FDA may convene an advisory committee of external experts to consider any of our other drug candidates, and the course and outcome of meetings with these advisory committees can be hard to predict;
- receive regulatory approvals from the FDA, EMA and similar foreign regulatory authorities;
- produce, through a validated process, in manufacturing facilities inspected and approved by regulatory authorities, including the FDA and EMA, sufficiently large quantities of the product candidate, and the related Botanical Drug Substances, or BDSs, to permit successful commercialization;
- build and maintain strong sales, distribution and marketing capabilities sufficient to launch commercial sales of our product candidates, or otherwise establish collaborations with third parties for the commercialization of our product candidates;
- obtain reimbursement from payers such as government health care programs and insurance companies and other third-party payers, as well as achieve commercially attractive levels of pricing;
- secure acceptance of our product candidates from physicians, health care payers, patients and the medical community;
- create positive publicity surrounding our product candidates;
- manage our spending as costs and expenses increase due to clinical trials and commercialization; and
- obtain and enforce sufficient intellectual property for our product candidates.

Our failure or delay with respect to any of the factors above could have a material adverse effect on our business, results of operations and financial condition.

We have limited marketing experience, and have only recently established our sales force, distribution and reimbursement capabilities, and we may not be able to successfully commercialize Epidiolex, or any of our product candidates if they are approved in the future.

Our ability to generate revenues ultimately depends on our ability to sell our approved products and secure adequate third-party reimbursement. We currently have limited experience in marketing and selling our products. Our product Sativex is currently approved and sold through marketing partners in a number of countries outside of the U.S. for treatment of MS spasticity. Epidiolex for treatment of LGS and Dravet syndrome in patients two years of age and older is our only product approved for sale in the U.S. and was approved for sale in Europe in September 2019, and we have only had commercialization experience in the U.S. since November 2018, and are only now building the commercial organization in Europe.

The commercial success of Epidiolex and nabiximols depends on a number of factors beyond our control, including the willingness of physicians to prescribe Epidiolex and nabiximols to patients, payers' willingness and ability to pay for the drug, the level of pricing achieved, patients' response to Epidiolex and nabiximols and the ability of our marketing partners to generate sales. There can be no guarantee that we will be able to establish or maintain the personnel, systems, arrangements and capabilities necessary to successfully commercialize Epidiolex, nabiximols or any product candidate approved by the FDA and EMA in the future. If we fail to establish or maintain successful marketing, sales and reimbursement capabilities or fail to enter into successful marketing arrangements with third parties, our product revenues may suffer.

If we are unable to effectively train and equip our sales force, our ability to successfully commercialize Epidiolex may be harmed.

We are and will continue to be required to expend significant time and resources to train our sales force to be credible, persuasive and compliant with applicable laws in marketing Epidiolex for the treatment of LGS and Dravet syndrome to physicians. In addition, we must continue to train our sales force to ensure that a consistent and appropriate message about Epidiolex is being delivered to our potential customers. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate potential customers about the benefits of Epidiolex and its proper administration, our efforts to successfully commercialize Epidiolex could be jeopardized, which would negatively impact our ability to generate product revenues.

We have recently grown our business and will need to further increase the size and complexity of our organization in the future, and we may experience difficulties in managing our growth and executing our growth strategy.

Our management and personnel, systems and facilities currently in place may not be adequate to support our business plan and future growth. With the FDA and the EMA approvals for Epidiolex and the decision to promote and market in the U.S. and Europe, the product candidates for which we receive marketing approval from the FDA and the EC, we have increased our number of full-time equivalent employees to 901 as of December 31, 2019 primarily because of the build out of our commercial team in the U.S. and Europe and significant ongoing investment in our pipeline. As a result of these activities, the complexity of our business operations has substantially increased, and we may need to further expand certain areas of our organization.

Our need to effectively manage our operations, growth and various projects requires that we:

- continue to improve our operational, financial, management and regulatory compliance controls and reporting systems and procedures;
- attract and retain sufficient numbers of talented employees;
- manage our commercialization activities effectively and in a cost-effective manner;
- manage our clinical trials effectively;
- manage our internal manufacturing operations effectively and in a cost-effective manner;
- manage our development efforts effectively while carrying out our contractual obligations to contractors and other third parties; and
- continue to improve our facilities.

In addition, historically, we have utilized and may continue to utilize the services of part-time outside consultants and contractors to perform a number of tasks for us, including tasks related to compliance programs, clinical trial management, regulatory affairs, formulation development and other drug development functions. Our growth strategy may entail expanding our use of consultants and contractors to implement these and other tasks going forward. If we are not able to effectively expand our organization by hiring new employees and expanding our use of consultants and contractors, we may be unable to successfully implement the tasks necessary to effectively execute on our planned research, development, manufacturing and commercialization activities and, accordingly, may not achieve our research, development and commercialization goals.

Our product candidates, if approved, may be unable to achieve the expected market acceptance and, consequently, limit our ability to generate revenue from new products.

Even when product development is successful and regulatory approval has been obtained, our ability to generate sufficient revenue depends on the acceptance of our products by physicians and patients. We cannot assure you that Epidiolex or nabiximols and our other product candidates will achieve the expected level of market acceptance and revenue if and when they obtain the requisite regulatory approvals. The market acceptance of any product depends on a number of factors, including the indication statement and warnings required by regulatory authorities in the product label. Market acceptance can also be influenced by continued demonstration of efficacy and safety in commercial use, physicians' willingness to prescribe the product, reimbursement from third-party payers such as government health care programs and private third-party payers, the price of the product, the nature of any post-approval risk, management activities mandated by regulatory authorities, competition, and marketing and distribution support. Further, our U.S. distribution depends on the adequate performance of a reimbursement support hub and contracted specialty pharmacies in a closed-distribution network. An ineffective or inefficient U.S. and European distribution model at launch may lead to the inability to fulfill demand, and consequently a loss of revenue. The success and acceptance of a product in one country may be negatively affected by our activities in another. If we fail to adapt our approach to clinical trials in the U.S. market to meet the needs of EMA or other European regulatory authorities, or to generate the health economics and outcomes research data needed to support pricing and reimbursement negotiations in Europe, we may have difficulties obtaining marketing authorization for our products from EMA and may have difficulties obtaining pricing and reimbursement approval for our products at a national level. Any factors preventing or limiting the market acceptance of our products could have a material adverse effect on our business, results of operations and financial condition.

In respect of our product candidates targeting rare indications, relevant regulatory exclusivities such as orphan drug exclusivity or pediatric exclusivity may not be granted or, if granted, may be limited.

The first NDA applicant with an Orphan Drug Designation for a particular active moiety to treat a specific disease or condition that receives FDA approval is usually entitled to a seven-year exclusive marketing period in the U.S. for that drug, for that indication. We rely in part on this orphan drug exclusivity and other regulatory exclusivities to protect Epidiolex and, potentially, our other products and product candidates from competitors, and we expect to continue relying in part on these regulatory exclusivities in the future. As to Epidiolex, the duration of our regulatory exclusivity period could be impacted by a number of factors, including the FDA's later determination that our request for orphan designation was materially defective, that the manufacturer is unable to supply sufficient quantities of the drug, that the extension of the exclusivity period established by the Improving Regulatory Transparency for New Medical Therapies Act does not apply, or the possibility that we are unable to successfully obtain pediatric exclusivity. There is no assurance that we will successfully obtain Orphan Drug Designation for other product candidates or other rare diseases or that a product candidate for which we receive Orphan Drug Designation will be approved, or that we will be awarded orphan drug exclusivity upon approval as, for example, the FDA may reconsider whether the eligibility criteria for such exclusivity have been met and/or maintained. Moreover, a drug product with an active moiety that is a different cannabinoid from that in our drug candidate or, under limited circumstances, the same drug product, may be approved by the FDA for the same indication during the period of marketing exclusivity. The limited circumstances include a showing that the second drug is clinically superior to the drug with marketing exclusivity through a demonstration of superior safety or efficacy or that it makes a major contribution to patient care. In addition, if a competitor obtains approval and marketing exclusivity for a drug product with an active moiety that is the same as that in a product candidate we are pursuing for the same indication before us, approval of our product candidate would be blocked during the period of marketing exclusivity unless we could demonstrate that our product candidate is clinically superior to the approved product. In addition, if a competitor obtains approval and marketing exclusivity for a drug product with an active moiety that is the same as that in a product candidate we are pursuing for a different orphan indication, this may negatively impact the market opportunity for our product candidate. There have been legal challenges to aspects of the FDA's regulations and policies concerning the exclusivity provisions of the Orphan Drug Act, including whether two drugs are the same drug product, and future challenges could lead to changes that affect the protections potentially afforded our products in ways that are difficult to predict. In a recent successful legal challenge, a court invalidated the FDA's denial of orphan exclusivity to a drug on the grounds that the drug was not proven to be clinically superior to a previously approved product containing the same ingredient for the same orphan use. In response to the decision, the FDA released a policy statement stating that the court's decision is limited just to the facts of that particular case and that the FDA will continue to require the sponsor of a designated drug that is the "same" as a previously approved drug to demonstrate that its drug is clinically superior to that drug upon approval in order to be eligible for orphan drug exclusivity, or in some cases, to even be eligible for marketing approval. In the future, there is the potential for additional legal challenges to the FDA's orphan drug regulations and policies, and it is uncertain how such challenges might affect our business.

In the European Union, if a marketing authorization is granted for a medicinal product that is designated an orphan drug, that product is entitled to ten years of marketing exclusivity. During the period of marketing exclusivity, subject to limited exceptions, no similar medicinal product may be granted a marketing authorization for the orphan indication. There is no assurance that we will successfully obtain Orphan Drug Designation for future rare indications or orphan exclusivity upon approval of any of our product candidates that have already obtained designation. Even if we obtain orphan exclusivity for any product candidate, the exclusivity period can be reduced to six years if at the end of the fifth year it is established that the orphan designation criteria are no longer met or if it is demonstrated that the orphan drug is sufficiently profitable that market exclusivity is no longer justified. Further, a similar medicinal product may be granted a marketing authorization for the same indication notwithstanding our marketing exclusivity if we are unable to supply sufficient quantities of our product, or if the second product is safer, more effective or otherwise clinically superior to our orphan drug. In addition, if a competitor obtains marketing authorization and orphan exclusivity for a product that is similar to a product candidate we are pursuing for the same indication, approval of our product candidate would be blocked during the period of orphan marketing exclusivity unless we could demonstrate that our product candidate is safer, more effective or otherwise clinically superior to the approved product.

If the price for Epidiolex, nabiximols or any future approved products decreases or if governmental and other third-party payers do not provide coverage and adequate reimbursement levels, our revenue and prospects for profitability will suffer.

Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payers to reimburse all or part of the costs associated with their prescription drugs. Reimbursement systems in international markets vary significantly by country and by region, and reimbursement approvals generally must be obtained on a country-by-country basis. Coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payers is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower-cost therapeutic alternatives are already available or subsequently become available. Even if we obtain coverage for Epidiolex, nabiximols or other products we may market, the resulting reimbursement payment rates may require co-payments that patients find unacceptably high. Patients may not use Epidiolex or nabiximols if coverage is not provided or reimbursement is inadequate to cover a significant portion of its cost.

In addition, the market for Epidiolex and nabiximols will depend significantly on access to third-party payers' drug formularies, or lists of medications for which third-party payers' provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payers may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available, even if not approved for the indication for which Epidiolex or nabiximols is approved.

Third-party payers, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. The current environment is putting pressure on companies to price products below what they may feel is appropriate. Selling Epidiolex and nabiximols at less than an optimized price could impact our revenues and overall success as a company. We do not know if the price we have selected for Epidiolex or nabiximols is the optimized price. In addition, in the U.S., no uniform policy of coverage and reimbursement for drug products exists among third-party payers. Therefore, coverage and reimbursement for Epidiolex may differ significantly from payer to payer. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of Epidiolex or nabiximols to each payer separately, with no assurance that coverage will be obtained. If we are unable to obtain coverage of, and adequate payment levels for, Epidiolex, nabiximols or any other products we may market to third-party payers, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize Epidiolex, nabiximols or any other products we may market, and thereby adversely impact our profitability, results of operations, financial condition and future success.

In addition, where we have chosen to collaborate with a third party on product candidate development and commercialization, our partner may elect to reduce the price of our products in order to increase the likelihood of obtaining reimbursement approvals. In many countries, products cannot be commercially launched until reimbursement is approved and the negotiation process in some countries can exceed 12 months. In addition, pricing and reimbursement decisions in certain countries can be affected by decisions taken in other countries, which can lead to mandatory price reductions and/or additional reimbursement restrictions across a number of other countries, which may thereby adversely affect our sales and profitability. In the event that countries impose prices that are not sufficient to allow us or our partners to generate a profit, our partners may refuse to launch the product in such countries or withdraw the product from the market, which would adversely affect sales and profitability. Events, such as price decreases, government mandated rebates or unfavorable reimbursement decisions, could affect the pricing and reimbursement of Epidiolex and our other product candidates and could have a material adverse effect on our business, reputation, results of operations and financial condition.

We expect to face intense competition, often from companies with greater resources and experience than we have.

The pharmaceutical industry is highly competitive and subject to rapid change. The industry continues to expand and evolve as an increasing number of competitors and potential competitors enter the market. Many of these competitors and potential competitors have substantially greater financial, technological, managerial and research and development resources and experience than we have. Some of these competitors and potential competitors have more experience than we have in the development of pharmaceutical products, including validation procedures and regulatory matters. In addition, Epidiolex and nabiximols compete with, and our product candidates, if successfully developed, will compete with, product offerings from large and well-established companies that have greater marketing and sales experience and capabilities than we or our collaboration partners have. Zogenix, Inc submitted their NDA for low-dose fenfluramine (Fintepla) in Dravet syndrome in September 2019. Ovid Therapeutics Inc./Takeda Pharmaceutical Company Limited and Marinus Pharmaceuticals, Inc. are developing therapies for treating Developmental and Epileptic Encephalopathies (includes Dravet and LGS). Biocodex received regulatory approval from the FDA for the drug Stiripentol (Diacomit) for the treatment of Dravet syndrome in September 2018. Other companies, including those with greater resources than us may announce similar plans in the future. In addition, there are non-FDA approved CBD preparations being made available from companies in the medical marijuana industry, which might attempt to compete with Epidiolex. If we are unable to compete successfully, our commercial opportunities will be reduced and our business, results of operations and financial conditions may be materially harmed.

Product shipment delays could have a material adverse effect on our business, results of operations and financial condition.

The shipment, import and export of Epidiolex, nabiximols and our other product candidates require import and export licenses. In the U.S., the FDA, U.S. Customs and Border Protection and the DEA, and in the U.K., the Home Office, and in other countries, similar regulatory authorities regulate the import and export of pharmaceutical products that contain controlled substances, including Epidiolex, nabiximols and our other product candidates. Specifically, the import and export process requires the issuance of import and export licenses by the relevant controlled substance authority in both the importing and exporting country. We may not be granted, or if granted, maintain, such licenses from the authorities in certain countries. Even if we obtain the relevant licenses, shipments of Epidiolex, nabiximols and our product candidates may be held up in transit, which could cause significant delays and may lead to product batches being stored outside required temperature ranges. Inappropriate storage may damage the product shipment resulting in a partial or total loss of revenue from one or more shipments of Epidiolex, nabiximols or our other product candidates. A partial or total loss of revenue from one or more shipments of Epidiolex, nabiximols or our other product candidates could have a material adverse effect on our business, results of operations and financial condition.

Problems in our manufacturing process, failure to comply with manufacturing regulations or unexpected increases in our manufacturing costs could harm our business, results of operations and financial condition.

We are responsible for the manufacture and supply of nabiximols to our collaboration partners and for the manufacture and supply of Epidiolex, nabiximols and other product candidates for commercial use and for use in clinical trials. The manufacturing of Epidiolex, nabiximols and our product candidates necessitates compliance with GMP and other regulatory requirements in jurisdictions internationally. Our ability to successfully manufacture Epidiolex, nabiximols and other product candidates involves cultivation of botanical raw material from specific cannabinoid plants, extraction and purification processes, manufacture of finished products and labeling and packaging, which includes product information, tamper evidence and anti-counterfeit features, under tightly controlled processes and procedures. For Epidiolex, nabiximols and our product candidates, production also requires the cultivation of cannabinoid plants under highly controlled and standardized conditions. In addition, we must ensure chemical consistency among our batches, including clinical batches and, if approved, marketing batches. Demonstrating such consistency may require typical manufacturing controls as well as clinical data. We must also ensure that our batches conform to complex release specifications. For each step in the manufacturing process for nabiximols, we are currently reliant on single manufacturing facilities and no back-up facilities are yet in place. We have a second site at which we can grow the specific cannabinoid plants that produce the CBD used in Epidiolex, a second site at which we can extract CBD from botanical raw material and a second site at which we can crystallize the purified CBD from the liquid plant extract, but we are currently reliant on a single manufacturing facility, and no back-up facilities are yet in place, for the other steps in the Epidiolex production process. Because nabiximols is a complex mixture manufactured from plant materials, and because the release specifications may not be identical in all countries, certain batches may fail release testing and not be able to be commercialized. A number of our product candidates (excluding Epidiolex) also consist of a complex mixture manufactured from plant materials, and are therefore subject to a similar risk. If we are unable to manufacture Epidiolex, nabiximols or other product candidates in accordance with regulatory specifications, including GMP, or if there are disruptions in our manufacturing process due to damage, loss or otherwise, or failure to pass regulatory inspections of our manufacturing facilities, we may not be able to meet current demand or supply sufficient product for use in clinical trials, and this may also harm our ability to commercialize Epidiolex, nabiximols and our product candidates on a timely or cost-competitive basis, if at all. We have an on-going program for expanding and upgrading parts of our growing and manufacturing facilities and we are working with a number of contract manufacturing partners. This has allowed us to implement a manufacturing program that we believe includes a sufficient number of growing and manufacturing sites that should provide sufficient quantities to meet initial demand, and meet the FDA's and EMA's stringent requirements for demonstrating equivalence of the scaled-up manufacturing process. This program requires significant time

and resources and may not be successful. We are in the final stages of significantly expanding our growing facilities to meet potential peak demand for Epidiolex, including working with several new contractor manufacturers and adopting new methods in order to handle and process bulk quantities of botanical raw material. We are planning to increase the scale at which we manufacture Epidiolex over the next few years in order to meet potential peak demand for Epidiolex, including working with several new contractors and, potentially, adopting new processes. These activities may be unsuccessful, may lead to delays, interruptions to supply or may prove to be more costly than anticipated.

We may fail to expand our growing and manufacturing capability in time to meet market demand for our products and product candidates, and the FDA and EMA may refuse to accept our facilities or those of our contract manufactures as being suitable for the production of our products and product candidates. Any problems in our growing or manufacturing process could have a material adverse effect on our business, results of operations and financial condition.

In addition, before we can begin commercial manufacture of any product candidates for sale in the U.S. or in Europe, we must obtain FDA and EMA regulatory approval for the product, which requires a successful FDA and EMA inspection of our manufacturing facilities and those of our contract manufacturers, processes and quality systems in addition to other product-related approvals. Although we successfully navigated this pre-approval inspection process as it relates to Epidiolex in the U.S. and in Europe, pharmaceutical manufacturing facilities are continuously subject to post-approval inspection by the FDA, EMA and foreign regulatory authorities. Due to the complexity of the processes used to manufacture our product candidates, we may be unable to initially or continue to pass federal, state or international regulatory inspections in a cost-effective manner. If we are unable to comply with manufacturing regulations, we may be subject to fines, unanticipated compliance expenses, recall or seizure of any approved products, total or partial suspension of production and/or enforcement actions, including injunctions, and criminal or civil prosecution. These possible sanctions would adversely affect our business, results of operations and financial condition.

Further, the processes we use for cultivation of botanical raw material and the production of product candidates for use in clinical trials may be different from the processes we use to produce commercial product and/or may not be capable of producing sufficient quantities of product for commercial purposes. We may therefore need to undertake additional manufacturing process development and scale-up activities before we can commercialize a product. This may include the conduct of bioequivalence studies to demonstrate that product produced by the process used to manufacture on a commercial scale is the same as the material used in clinical trials. If we cannot demonstrate that our commercial scale product is the same as material used in our clinical trials, we may not be permitted to sell that product, which could have an impact on our business, results of operations and financial condition.

Product recalls or inventory losses caused by unforeseen events, cold chain interruption and testing difficulties may adversely affect our operating results and financial condition.

Epidiolex, nabiximols and our product candidates are manufactured and distributed using technically complex processes requiring specialized facilities, highly specific raw materials and other production constraints. The complexity of these processes, as well as strict company and government standards for the manufacture of our products, subjects us to production risks. While product batches released for use in clinical trials or for commercialization undergo sample testing, some defects may only be identified following product release. Some of our products must be stored and transported at temperatures within a certain range, which is known as “strict cold chain” storage and transportation. The occurrence or suspected occurrence of production and distribution difficulties can lead to lost inventories, and in some cases product recalls, with consequential reputational damage and the risk of product liability. The investigation and remediation of any identified problems can cause production delays, substantial expense, lost sales and delays of new product launches.

Epidiolex, nabiximols and our product candidates contain controlled substances, the use of which may generate public controversy.

Since Epidiolex, nabiximols and our other product candidates contain controlled substances, their regulatory approval may generate public controversy. Political and social pressures and adverse publicity could lead to delays in approval of, and increased expenses for, Epidiolex, nabiximols and our product candidates. These pressures could also limit or restrict the introduction and marketing of Epidiolex, nabiximols and our product candidates. Adverse publicity from cannabis misuse or adverse side effects from cannabis or other cannabinoid products may adversely affect the commercial success or market penetration achievable by Epidiolex, nabiximols and our product candidates. The nature of our business attracts a high level of public and media interest, and in the event of any resultant adverse publicity, our reputation may be harmed.

Business interruptions could delay us in the process of developing our product candidates and could disrupt our product sales.

Loss of our manufacturing facilities, our growing facilities, stored inventory or laboratory facilities through fire, theft or other causes, or loss of our botanical raw material due to pathogenic infection or other causes, could have an adverse effect on our ability to meet demand for Epidiolex or nabiximols or to continue product development activities and to conduct our business. Failure to supply our partners with commercial product may lead to adverse consequences, including the right of partners to take over responsibility for product supply. We currently have insurance coverage to compensate us for such business interruptions; however, such coverage may prove insufficient to fully compensate us for the damage to our business resulting from any significant property or casualty loss to our inventory or facilities.

We have significant and increasing liquidity needs and may require additional funding.

Our operations have consumed substantial amounts of cash since inception. For the year ended December 31, 2019, we reported a net operating cash outflow of $123.5 million and a net cash inflow from investing activities of $61.6 million.

Research and development, sales, general and administrative expenses and cash used for operations will continue to be significant and may increase substantially in the future in connection with new research and development initiatives and continued product commercialization efforts. We may need to raise additional capital to fund our operations, continue to conduct clinical trials to support potential regulatory approval of marketing applications and to fund commercialization of our products.

The amount and timing of our future funding requirements will depend on many factors, including, but not limited to:

- the timing of FDA approval, if any, and approvals in international markets of our product candidates, if at all;
- the timing and amount of revenue from sales of our products, or revenue from grants or other sources;
- the rate of progress and cost of our clinical trials and other product development programs;
- costs of establishing or outsourcing sales, marketing and distribution capabilities;
- costs and timing of completion of expanded in-house manufacturing facilities as well as any outsourced growing and commercial manufacturing supply arrangements for our product candidates;
- costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with our product candidates;
- costs of operating as a U.S. public company;
- the effect of competing technological and market developments;
- personnel, facilities and equipment requirements; and
- the terms and timing of any additional collaborative, licensing, co-promotion or other arrangements that we may establish.

While we expect to fund our future capital requirements from a number of sources including existing cash balances, future cash flows from operations and the proceeds from further public offerings, we cannot assure you that any of these funding sources will be available to us on favorable terms, or at all. Further, even if we can raise funds from all of the above sources, the amounts raised may not be sufficient to meet our future capital requirements.

Operating results may vary significantly in future periods.

Our quarterly revenues, expenses and operating results have fluctuated in the past and are likely to fluctuate significantly in the future. Our financial results are unpredictable and may fluctuate, for among other reasons, due to:

- commercial sales of Epidiolex and Sativex;
- our achievement of product development objectives and milestones;
- clinical trial enrollment and expenses;
- research and development expenses; and
- the timing and nature of contract manufacturing and contract research payments.

A high portion of our costs are predetermined on an annual basis, due in part to our significant research and development costs. Thus, small declines in revenue could disproportionately affect financial results in a quarter. Because of these factors, our financial results in one or more future quarters may fail to meet the expectations of securities analysts or investors, which could cause our share price to decline.

If product liability lawsuits are successfully brought against us, we will incur substantial liabilities and may be required to limit the commercialization of Epidiolex, Sativex and our product candidates.

Although we have never had any product liability claims or lawsuits brought against us, we face potential product liability exposure related to the testing of our product candidates in human clinical trials, and we currently face exposure to claims in jurisdictions where we currently or potentially market and distribute our products. We may face exposure to claims by an even greater number of persons as we market and distribute our products commercially in the U.S., Europe and elsewhere. Now, and in the future, an individual may bring a liability claim against us alleging that Epidiolex, Sativex or one of our product candidates caused an injury. While we continue to take what we believe are appropriate precautions, we may be unable to avoid significant liability if any product liability lawsuit is brought against us. Large judgments have been awarded in class action or individual lawsuits based on drugs that had unanticipated side effects. Although we have purchased insurance to cover product liability lawsuits, if we cannot successfully defend ourselves against product liability claims, or if such insurance coverage is inadequate, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for Epidiolex, Sativex and our product candidates if such product candidates are approved;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs of related litigation;
- substantial monetary awards to patients and others;
- increased cost of liability insurance;
- loss of revenue; and
- the inability to successfully commercialize our products.

Counterfeit versions of our products could harm our business.

Counterfeiting activities and the presence of counterfeit products in a number of markets and over the Internet continue to be a challenge for maintaining a safe drug supply for the pharmaceutical industry. Counterfeit products are frequently unsafe or ineffective and can be life-threatening. To distributors and users, counterfeit products may be visually indistinguishable from the authentic version. Reports of adverse reactions to counterfeit drugs along with increased levels of counterfeiting could be mistakenly attributed to the authentic product, affect patient confidence in the authentic product and harm the business of companies such as ours. If our products were to be the subject of counterfeits, we could incur reputational and financial harm.

We depend upon our key personnel and our ability to attract and retain employees.

Our future growth and success depend on our ability to recruit, retain, manage and motivate our employees. The inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results. Due to the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific, technical and managerial personnel. The competition for qualified personnel in the pharmaceutical field is intense. Due to this intense competition, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA or EMA regulations, provide accurate information to the FDA or EMA, comply with applicable manufacturing standards, comply with other foreign, federal and state laws and regulations, report information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information, including information obtained in the course of clinical trials, or illegal appropriation of drug product, which could result in government investigations and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct. The precautions we take to detect and prevent these prohibited activities may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

If we are unable to use net operating loss carry-forwards and certain built-in losses to reduce future tax payments, or benefit from favorable tax legislation, our business, results of operations and financial condition may be adversely affected.

As a U.K. resident trading company, we are predominantly subject to U.K. corporate taxation. At December 31, 2019, we had cumulative carry-forward tax losses of $626.0 million, available to offset against future profits (subject to the restrictions on the use of such losses described below). The majority of these tax loss attributes have not been recognized on our balance sheet at December 31, 2019. It should be noted, however, that the use of carry-forward losses is restricted such that they are not available for offset against more than 50% of taxable profits in any accounting period (subject to a £5 million annual allowance). Additionally, as we carry out extensive research and development activities in the U.K., we benefit from the U.K. research and development tax credit regime. We have benefitted from the U.K. research and development tax credit regime for small and medium-sized companies, whereby our principal research subsidiary, GW Research Ltd, was able to surrender a portion of available losses that arise from research and development activity for a refundable credit of up to approximately 33.4% of the eligible research and development expenditure. However, due to the increase in the size of our employee workforce in the U.K. and our annual turnover we are now subject to the U.K. research and development tax credit regime for large companies. Beginning October 1, 2017, GW Research Ltd is able to claim a refundable research and development expenditure credit, but that credit is payable at a lower effective rate of approximately 9.7%. We may also benefit in the future from the U.K.'s "patent box" regime, which would allow certain profits attributable to revenue from patented products to be taxed at a lower rate of 10%. When taken in combination with our available carry-forward tax losses and the enhanced relief available on our research and development expenditure, we expect that this may result in a long-term low rate of corporation tax. If, however, we are unable to generate sufficient future taxable profits, or for any reason to utilize our carry-forward losses (as currently restricted), or there are unexpected adverse changes to the U.K. research and development tax credit regime or "patent box" regime, or we are unable to qualify for such advantageous tax legislation, our business, results of operations and financial condition may be adversely affected.

We are subject to the U.K. Bribery Act, the U.S. Foreign Corrupt Practices Act and other anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act, the U.S. Foreign Corrupt Practices Act, or FCPA, and other anti-corruption laws that apply in countries where we do business. The Bribery Act, FCPA and these other laws generally prohibit us and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. Additionally, under the Bribery Act there could be an offense if we failed to prevent a third party from committing bribery in the performance of services for us or on our behalf. We and our commercial partners operate in a number of jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the U.K. and the U.S., and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

However, there is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by the U.K., the U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

Our proprietary information, or that of our customers, suppliers and business partners, may be lost or we may suffer security breaches.

In the ordinary course of our business, we collect and store sensitive data, including valuable and commercially sensitive intellectual property, clinical trial data, our proprietary business information and that of our customers, suppliers and business partners, and personally identifiable information of our customers, clinical trial subjects and employees, and patients, in our data centers, on our networks, and with our third-party cloud service providers. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure, and that of our third parties, may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. 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 could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, regulatory penalties, disrupt our operations, damage our reputation and cause a loss of confidence in our products and our ability to conduct clinical trials, which could adversely affect our business and reputation and lead to delays in gaining regulatory approvals for Epidiolex. Although we maintain business interruption insurance coverage, our insurance might not cover all losses from any future breaches of our systems.

Failure of our information technology systems, including cybersecurity attacks or other data security incidents, could significantly disrupt the operation of our business.

Our business increasingly depends on the use of information technologies, which means that certain key areas such as research and development, production and sales are to a large extent dependent on our information systems or those of third-party providers. Our ability to execute our business plan and to comply with regulators' requirements with respect to data control and data integrity depends, in part, on the continued and uninterrupted performance of our information technology systems, or IT systems and the IT systems supplied by third-party service providers. As information systems and the use of software and related applications by us, our business partners, suppliers and customers become more cloud-based, there has been an increase in global cybersecurity vulnerabilities and threats, including more sophisticated and targeted cyber-related attacks that pose a risk to the security of our information systems and networks and the confidentiality, availability and integrity of data and information. In addition, our IT systems are vulnerable to damage from a variety of sources, including telecommunications or network failures, malicious human acts and natural disasters. Moreover, despite network security and backup measures, some of our servers are potentially vulnerable to physical or electronic break-ins, computer viruses and similar disruptive problems. Despite the precautionary measures we and our third-party service providers have taken to prevent unanticipated problems that could affect our IT systems, a successful cybersecurity attack or other data security incident could result in the misappropriation and/or loss of confidential or personal information, create system interruptions or deploy malicious software that attacks our systems. It is also possible that a cybersecurity attack might not be noticed for some period of time. In addition, sustained or repeated system failures or problems arising during the upgrade of any of our IT systems that interrupt our ability to generate and maintain data, and in particular to operate our proprietary technology platform, could adversely affect our ability to operate our business. The occurrence of a cybersecurity attack or incident could result in business interruptions from the disruption of our information technology systems, or negative publicity resulting in reputational damage with our shareholders and other stakeholders and/or increased costs to prevent, respond to or mitigate cybersecurity events. In addition, the unauthorized dissemination of sensitive personal information or proprietary or confidential information could expose us or other third parties to regulatory fines or penalties, litigation and potential liability, or otherwise harm our business

Security breaches, loss of data and other disruptions could compromise sensitive information related to our business, prevent us from accessing critical information or expose us to liability, which could adversely affect our business and our reputation.

In the ordinary course of our business, we, our vendors, and our third-party cloud service providers collect and store sensitive data, including legally protected patient health information, credit card information, personally identifiable information about our employees and patients, intellectual property, and proprietary business information. We manage and maintain our applications and data utilizing cloud-based and on-site systems. These applications and data encompass a wide variety of business critical information including research and development information, commercial information and business and financial information.

The secure processing, storage, maintenance and transmission of this critical information is vital to our operations and business strategy, and we devote significant resources to protecting such information. Although we take measures to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure may be vulnerable to attacks by hackers, or viruses, breaches or interruptions due to employee error, malfeasance or other disruptions, or lapses in compliance with privacy and security mandates. Any such virus, breach or interruption could compromise our networks and the information stored there could be accessed by unauthorized parties, publicly disclosed, lost or stolen. We have measures in place that are designed to prevent, and if necessary to detect and respond to such security incidents, breaches of privacy, and security mandates. However, in the future, any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, such as HIPAA and General Data Protection Regulation, or GDPR, government enforcement actions and regulatory penalties. Unauthorized access, loss or dissemination could also disrupt our operations, including our ability to process samples, provide test results, share and monitor safety data, bill payers or patients, provide customer support services, conduct research and development activities, process and prepare company financial information, manage various general and administrative aspects of our business and may damage our reputation, any of which could adversely affect our business, financial condition and results of operations.

In May 2016, the European Union formally adopted the GDPR, which applies to all European Union member states from May 25, 2018 and replaced the European Union Data Protection Directive. The regulation introduces stringent new data protection requirements in the European Union and substantial fines for breaches of the data protection rules. It has increased our responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with the new European Union data protection rules. The GDPR is a complex law and the regulatory guidance is still evolving, including with respect to how the GDPR should be applied in the context of clinical trials or other transactions from which we may gain access to personal data. These changes in the law will increase our costs of compliance and result in greater legal risks.

Legislative or regulatory reform of the health care system in the U.S. and foreign jurisdictions may affect our ability to profitably sell our products, if approved.

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

Specifically, in both the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the health care system in ways that could affect our ability to sell our products profitably. For example, certain states in the U.S. are proposing legislation mandating publicly funded health program coverage of medical cannabis. In addition, the 2010 Affordable Care Act, or the ACA, substantially changed the way healthcare is financed by both governmental and private insurers. Both Congress and the U.S. President have already taken some actions that are intended to limit significantly the ACA, and we expect efforts to further modify or repeal the ACA to continue. The success and potential effects of these efforts to repeal or modify the ACA are not clear.

We expect additional federal and state legislative proposals for health care reform, which could limit the prices that can be charged for the products we develop and may limit our commercial opportunity.

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

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

We may acquire other companies which could divert our management's attention, result in additional dilution to our shareholders and otherwise disrupt our operations and harm our operating results.

We may in the future seek to acquire businesses, products or technologies that we believe could complement or expand our product offerings, enhance our technical capabilities or otherwise offer growth opportunities. The pursuit of potential acquisitions may divert the attention of management and cause us to incur various expenses in identifying, investigating and pursuing suitable acquisitions, whether or not they are consummated. If we acquire additional businesses, we may not be able to integrate the acquired personnel, operations and technologies successfully, effectively manage the combined business following the acquisition or realize anticipated cost savings or synergies. We also may not achieve the anticipated benefits from the acquired business due to a number of factors, including:

- incurrence of acquisition-related costs;
- diversion of management's attention from other business concerns;

- unanticipated costs or liabilities associated with the acquisition;
- harm to our existing business relationships with collaboration partners as a result of the acquisition;
- harm to our brand and reputation;
- the potential loss of key employees;
- use of resources that are needed in other parts of our business; and
- use of substantial portions of our available cash to consummate the acquisition.

In the future, if our acquisitions do not yield expected returns, we may be required to take charges to our operating results arising from the impairment assessment process. Acquisitions may also result in dilutive issuances of equity securities or the incurrence of debt, which could adversely affect our operating results. In addition, if an acquired business fails to meet our expectations, our business, results of operations and financial condition may be adversely affected.

The United Kingdom's withdrawal from the European Union could lead to increased market volatility, which could adversely impact the market price of our ADSs and make it more difficult for us to do business in Europe or have other adverse effects on our business.

The United Kingdom officially left the European Union as a member state on January 31, 2020 and now has third country status. There now follows a transitional period during which the U.K. and the EU will attempt to conclude a free trade agreement (the "Transitional Period"). During the Transitional Period, the U.K. will abide by all EU laws and regulations. In the event that the U.K. and the EU cannot agree to the terms of such a free trade agreement, the Transitional Period will end on the December 31, 2020 unless an extension to this date is agreed. In the event that no free trade agreement is reached by the end of 2020, it is likely that cross-border trade between the United Kingdom and the EU will revert to world trade organization terms. Our distribution model in the EU with the marketing authorization and a hub in the Netherlands has been designed to mitigate the impact of this on our business as much as possible. In addition, if no free trade agreement can be reached and the United Kingdom leaves the European Union with no free trade agreement, there will be a period of considerable uncertainty particularly in relation to United Kingdom financial and banking markets as well as on the regulatory process in Europe. As a result of this uncertainty, financial markets could experience volatility which could adversely affect the market price of our ADSs. We may also face new regulatory costs and challenges that could have a material adverse effect on our operations. In this regard, the EMA has already issued a notice reminding marketing authorization holders of centrally authorized medicinal products for human and veterinary use of certain legal requirements that need to be considered as part of Brexit, such as the requirement for the marketing authorization holder of a product centrally approved by the European Commission to be established in the European Union, and the requirement for some activities relating to centrally approved products, such as batch release and pharmacovigilance, to be performed in the European Union. As a result of the foregoing developments, and in the absence of any clear indication that any agreed form of a free trade agreement will contain a contrary requirement, we have taken steps to establish a network of subsidiary undertakings in the major European markets and have established pharmacovigilance and batch release operations in the European Union. Depending on the terms of Brexit, the United Kingdom could lose the benefits of global trade agreements negotiated by the European Union on behalf of its members, which may result in increased trade barriers which could make our doing business worldwide more difficult. In addition, currency exchange rates in the pound sterling and the euro with respect to each other and the U.S. dollar have already been adversely affected by Brexit. Should this foreign exchange volatility continue it could cause volatility in our financial results.

Risks Related to Development and Regulatory Approval of Epidiolex, Nabiximols and Our Product Candidates

Clinical trials for our product candidates are expensive, time-consuming, uncertain and susceptible to change, delay or termination. The results of clinical trials are open to differing interpretations.

Clinical trials are expensive, time consuming and difficult to design and implement. Regulatory agencies may analyze or interpret the results differently than us. Even if the results of our clinical trials are favorable, the clinical trials for a number of our product candidates are expected to continue for several years and may take significantly longer to complete. In addition, we, the FDA, EMA, or other regulatory authorities, including state and local authorities, or an Institutional Review Board, or IRB, with respect to a trial at its institution, may suspend, delay or terminate our clinical trials at any time, require us to conduct additional clinical trials, require a particular clinical trial to continue for a longer duration than originally planned, require a change to our development plans such that we conduct clinical trials for a product candidate in a different order, e.g., in a step-wise fashion rather than running two trials of the same product candidate in parallel, or the DEA could suspend or terminate the registrations and quota allotments we require in order to procure and handle controlled substances, for various reasons, including:

- lack of effectiveness of any product candidate during clinical trials;
- discovery of serious or unexpected toxicities or side effects experienced by trial participants or other safety issues, such as drug interactions, including those which cause confounding changes to the levels of other concomitant medications;
- slower than expected rates of subject recruitment and enrollment rates in clinical trials;
- difficulty in retaining subjects who have initiated a clinical trial but may withdraw at any time due to adverse side effects from the therapy, insufficient efficacy, fatigue with the clinical trial process or for any other reason;
- delays or inability in manufacturing or obtaining sufficient quantities of materials for use in clinical trials due to regulatory and manufacturing constraints;
- inadequacy of or changes in our manufacturing process or product formulation;
- delays in obtaining regulatory authorization to commence a trial, including “clinical holds” or delays requiring suspension or termination of a trial by a regulatory agency, such as the FDA, before or after a trial is commenced;
- DEA-related recordkeeping, reporting or security violations at a clinical site, leading the DEA or state authorities to suspend or revoke the site’s controlled substance license and causing a delay or termination of planned or ongoing trials;
- changes in applicable regulatory policies and regulation, including changes to requirements imposed on the extent, nature or timing of studies;
- delays or failure in reaching agreement on acceptable terms in clinical trial contracts or protocols with prospective clinical trial sites;
- uncertainty regarding proper dosing;
- delay or failure to supply product for use in clinical trials which conforms to regulatory specification;
- unfavorable results from ongoing pre-clinical studies and clinical trials;
- failure of our contract research organizations, or CROs, or other third-party contractors to comply with all contractual requirements or to perform their services in a timely or acceptable manner;
- failure by us, our employees, our CROs or their employees to comply with all applicable FDA or other regulatory requirements relating to the conduct of clinical trials or the handling, storage, security and recordkeeping for controlled substances;
- scheduling conflicts with participating clinicians and clinical institutions;
- failure to design appropriate clinical trial protocols;
- regulatory concerns with cannabinoid products generally and the potential for abuse;
- insufficient data to support regulatory approval;

- inability or unwillingness of medical investigators to follow our clinical protocols; or
- difficulty in maintaining contact with patients during or after treatment, which may result in incomplete data.

Any of the foregoing could have a material adverse effect on our business, results of operations and financial condition.

Any failure by us to comply with existing regulations could harm our reputation and operating results.

We are subject to extensive regulation by U.S. federal and state and foreign governments in each of the markets where we currently sell or plan to sell Epidiolex and nabiximols, as applicable, or in markets where we have product candidates progressing through the approval process.

We must also adhere to all regulatory requirements including FDA's Good Laboratory Practice, Good Clinical Practice, and Current Good Manufacturing Practices requirements, or cGMP, pharmacovigilance requirements, advertising and promotion restrictions, reporting and recordkeeping requirements, and their European equivalents. If we or our suppliers fail to comply with applicable regulations, including FDA pre-or post-approval cGMP requirements, then the FDA or other foreign regulatory authorities could sanction us. Even if a drug is FDA-approved, regulatory authorities may impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-marketing trials. Epidiolex, and any of our product candidates that may be approved in the U.S. in the future, will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, distribution, import, export, advertising, promotion, sampling, recordkeeping and submission of safety and other post-market information, including both federal and state requirements in the U.S. In addition, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to GMP. As such, we and our contract manufacturers (in the event contract manufacturers are appointed in the future) are subject to continual review and periodic inspections to assess compliance with GMP. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, quality control and quality assurance. We will also be required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of the product, it may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may:

- issue warning letters;
- impose civil or criminal penalties;
- suspend regulatory approval;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including by requiring us to enter into a Corporate Integrity Agreement or closing our contract manufacturers' facilities, if any; or
- seize or detain products or require a product recall.

In addition, our products are regulated by the DEA, under the Controlled Substances Act. DEA scheduling is a separate process that can delay when a drug may become available to patients beyond an NDA approval date, and the timing and outcome of such DEA process is uncertain. See also "Risks Related to Controlled Substances".

In addition, any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from Epidiolex, Sativex and our product candidates. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our business and our operating results may be adversely affected.

Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses, divert our management's attention from the operation of our business and damage our reputation. We expend significant resources on compliance efforts and such expenses are unpredictable and might adversely affect our results. Changing laws, regulations and standards might also create uncertainty, higher expenses and increase insurance costs. As a result, we intend to invest all reasonably necessary resources to comply with evolving standards, and this investment might result in increased management and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities.

We are subject to federal, state and foreign healthcare laws and regulations and implementation of or changes to such healthcare laws and regulations could adversely affect our business and results of operations.

In both the U.S. and certain foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell Epidiolex or Sativex, as applicable, and any other potential products. If we are found to be in violation of any of these laws or any other federal or state regulations, we may be subject to administrative, civil and/or criminal penalties, damages, fines, individual imprisonment, exclusion from federal health care programs and the restructuring of our operations. Any of these could have a material adverse effect on our business and financial results. Since many of these laws have not been fully interpreted by the courts, there is an increased risk that we may be found in violation of one or more of their provisions. Any action against us for violation of these laws, even if we ultimately are successful in our defense, will cause us to incur significant legal expenses and divert our management's attention away from the operation of our business.

In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with Epidiolex, and any other products we may market, which could negatively impact our profitability.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we may receive for any approved product, including Epidiolex. There have been judicial challenges to certain aspects of the ACA and numerous legislative attempts to repeal and/or replace the ACA in whole or in part, and we expect there will be additional challenges and amendments to the ACA in the future. At this time, the full effect that the ACA will have on our business in the future remains unclear. An expansion in the government's role in the U.S. healthcare industry may cause general downward pressure on the prices of prescription drug products, lower reimbursements or any other product for which we obtain regulatory approval, reduce product utilization and adversely affect our business and results of operations. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize Epidiolex or any other products for which we may receive regulatory approval.

There is a high rate of failure for drug candidates proceeding through clinical trials.

Generally, there is a high rate of failure for drug candidates proceeding through clinical trials. We may suffer significant setbacks in our clinical trials similar to the experience of a number of other companies in the pharmaceutical and biotechnology industries, even after receiving promising results in earlier trials. Further, even if we view the results of a clinical trial to be positive, the FDA or other regulatory authorities may disagree with our interpretation of the data. In the event that we obtain negative results from clinical trials for product candidates or other problems related to potential chemistry, manufacturing and control issues or other hurdles occur and our product candidates are not approved, we may not be able to generate sufficient revenue or obtain financing to continue our operations, our ability to execute on our current business plan may be materially impaired, our reputation in the industry and in the investment community might be significantly damaged and the price of our ADSs could decrease significantly. In addition, our inability to properly design, commence and complete clinical trials may negatively impact the timing and results of our clinical trials and ability to seek approvals for our drug candidates.

If we are found in violation of federal or state "fraud and abuse" laws, we may be required to pay a penalty and/or be suspended from participation in federal or state health care programs, which may adversely affect our business, financial condition and results of operations.

In the U.S., we are subject to various federal and state health care "fraud and abuse" laws, including anti-kickback laws, false claims laws and other laws intended to reduce fraud and abuse in federal and state health care programs, which could affect us particularly upon successful commercialization of our products in the U.S. The Medicare and Medicaid Patient Protection Act of 1987, or federal Anti-Kickback Statute, makes it illegal for any person, including a prescription drug manufacturer (or a party acting

on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce the referral of business, including the purchase, order or prescription of a particular drug for which payment may be made under a federal health care program, such as Medicare or Medicaid. Under federal law, some arrangements, known as safe harbors, are deemed not to violate the federal Anti-Kickback Statute. Although we seek to structure our business arrangements in compliance with all applicable requirements, it is often difficult to determine precisely how the law will be applied in specific circumstances. Accordingly, it is possible that our practices may be challenged under the federal Anti-Kickback Statute and Federal False Claims Act. Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including fines and/or exclusion or suspension from federal and state health care programs such as Medicare and Medicaid and debarment from contracting with the U.S. government. In addition, private individuals have the ability to bring actions on behalf of the government under the federal False Claims Act as well as under the false claims laws of several states.

Many states have adopted laws similar to the federal anti-kickback statute, some of which apply to the referral of patients for health care services reimbursed by any source, not just governmental payers. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement, we could be subject to penalties.

Neither the government nor the courts have provided definitive guidance on the application of fraud and abuse laws to our business. Law enforcement authorities are increasingly focused on enforcing these laws, and it is possible that some of our practices may be challenged under these laws. While we believe we have structured our business arrangements to comply with these laws, it is possible that the government could allege violations of, or convict us of violating, these laws. If we are found in violation of one of these laws, we could be required to pay a penalty and could be suspended or excluded from participation in federal or state health care programs, and our business, results of operations and financial condition may be adversely affected.

Our ability to research, develop and commercialize Epidiolex, nabiximols and our product candidates is dependent on our ability to maintain licenses relating to the cultivation, possession and supply of controlled substances.

Our research and manufacturing facilities are located exclusively in the United Kingdom. In the United Kingdom, licenses to cultivate, possess and supply cannabis for medical research are granted by the Home Office on an annual basis. Although the Home Office has renewed our licenses each year since 1998, it may not do so in the future, in which case we may not be in a position to carry on our research and development program in the United Kingdom. In addition, we are required to maintain our existing commercial licenses to cultivate, produce and supply cannabis. However, if the Home Office were not prepared to renew such licenses, we would be unable to manufacture and distribute our products on a commercial basis in the United Kingdom or beyond. In order to carry out research in countries other than the United Kingdom, similar licenses to those outlined above are required to be issued by the relevant authority in each country. In addition, we will be required to obtain licenses to export from the United Kingdom and to import into the recipient country. To date, we have obtained necessary import and export licenses to over 30 countries. Although we have an established track record of successfully obtaining such licenses as required, this may change in the future.

In the U.S., the DEA regulates the cultivation, possession and supply of cannabis for medical research and commercial development, including the requirement of annual registrations to manufacture or distribute pharmaceutical products derived from cannabis extracts. See also “Risks Related to Controlled Substances”.

Serious adverse events or other safety risks could require us to abandon development and preclude, delay or limit approval of our product candidates, limit the scope of any approved label or market acceptance, or cause the recall or loss of marketing approval of products that are already marketed.

If Epidiolex, nabiximols or any of our product candidates prior to or after any approval for commercial sale, cause serious or unexpected side effects, or are associated with other safety risks such as misuse, abuse or diversion, a number of potentially significant negative consequences could result, including:

- regulatory authorities may interrupt, delay or halt clinical trials;
- regulatory authorities may deny regulatory approval of our product candidates;
- regulatory authorities may require certain labeling statements, such as warnings or contraindications or limitations on the indications for use, and/or impose restrictions on distribution in the form of a REMS in connection with approval or post-approval;
- regulatory authorities may withdraw their approval, require more onerous labeling statements, impose a more restrictive REMS, or require us to recall any product that is approved;
- we may be required to change the way the product is administered or conduct additional clinical trials;
- our relationships with our collaboration partners may suffer;

- we could be sued and held liable for harm caused to patients; or
- our reputation may suffer. The reputational risk is heightened with respect to those of our product candidates that are being developed for pediatric indications.

We may voluntarily suspend or terminate our clinical trials if at any time we believe that they present an unacceptable risk to participants or if preliminary data demonstrate that our product candidates are unlikely to receive regulatory approval or unlikely to be successfully commercialized. Following receipt of approval for commercial sale of a product we may voluntarily withdraw or recall that product from the market if at any time we believe that its use, or a person's exposure to it, may cause adverse health consequences or death. To date we have not withdrawn, recalled or taken any other action, voluntary or mandatory, to remove an approved product from the market. To date, we have only voluntarily suspended clinical trials when recruitment of the target patients has proven to be too difficult or, temporarily, to properly investigate suspected adverse events. In addition, regulatory agencies, IRBs or data safety monitoring boards may at any time recommend the temporary or permanent discontinuation of our clinical trials or request that we cease using investigators in the clinical trials if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, or that they present an unacceptable safety risk to participants. Although we have never been asked by a regulatory agency, IRB or data safety monitoring board to temporarily or permanently discontinue a clinical trial, if we elect or are forced to suspend or terminate a clinical trial of any of our product candidates, the commercial prospects for that product will be harmed and our ability to generate product revenue from that product may be delayed or eliminated. Furthermore, any of these events may result in labeling statements such as warnings or contraindications. In addition, such events or labeling could prevent us or our partners from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our product candidates and impair our ability to generate revenue from the commercialization of these products either by us or by our collaboration partners.

The development of a REMS for Epidiolex or our product candidates could cause delays in the approval process and would add additional layers of regulatory requirements that could impact our ability to commercialize our product candidates in the U.S. and reduce their market potential.

Although the FDA approved our NDA for Epidiolex without requiring a REMS as a condition of approval of the NDA, the FDA may, post-approval, require a REMS for Epidiolex if it becomes aware of new safety information that makes a REMS necessary to ensure that the benefits of the drug outweigh the potential risks. REMS elements can include medication guides, communication plans for health care professionals, and ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. We may be required to adopt a REMS for our product candidates to ensure that the benefits outweigh the risks of abuse, misuse, diversion and other potential safety concerns. There can be no assurance that the FDA will approve a manageable REMS for our product candidates, which could create material and significant limits on our ability to successfully commercialize our product candidates in the U.S. Delays in the REMS approval process could result in delays in the NDA approval process. In addition, as part of the REMS, the FDA could require significant restrictions, such as restrictions on the prescription, distribution and patient use of the product, which could significantly impact our ability to effectively commercialize our product candidates, and dramatically reduce their market potential thereby adversely impacting our business, financial condition and results of operations. Even if initial REMS are not highly restrictive, if, after launch, our product candidates were to be subject to significant abuse/non-medical use or diversion from licit channels, this could lead to negative regulatory consequences, including a more restrictive REMS.

Risks Related to Our Reliance Upon Third Parties

Our existing collaboration arrangements and any that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize Epidiolex, nabiximols and our product candidates.

We are a party to, and may seek additional, collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of Epidiolex, nabiximols and our product candidates. We may, with respect to our product candidates, enter into new arrangements on a selective basis depending on the merits of retaining commercialization rights for ourselves as compared to entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies for each product candidate, both in the U.S. and internationally. To the extent that we decide to enter into collaboration agreements, we will face significant competition in seeking appropriate collaborators and the terms of any collaboration or other arrangements that we may establish may not be favorable to us.

Any existing or future collaboration that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding development, intellectual property, regulatory or commercialization matters can lead to delays in the development process or commercialization of the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Any such termination or expiration could harm our business reputation and may adversely affect us financially.

We depend on a limited number of suppliers for materials and components required to manufacture Epidiolex, nabiximols and our product candidates. The loss of these suppliers, or their failure to supply us on a timely basis, could cause delays in our current and future capacity and adversely affect our business.

We depend on a limited number of suppliers for the materials and components required to manufacture Epidiolex, nabiximols and our product candidates. As a result, we may not be able to obtain sufficient quantities of critical materials and components in the future. A delay or interruption by our suppliers may also harm our business, results of operations and financial condition. In addition, the lead time needed to establish a relationship with a new supplier can be lengthy, and we may experience delays in meeting demand in the event we must switch to a new supplier. The time and effort to qualify for and, in some cases, obtain regulatory approval for a new supplier could result in additional costs, diversion of resources or reduced manufacturing yields, any of which would negatively impact our operating results. Our dependence on single-source suppliers exposes us to numerous risks, including the following: our suppliers may cease or reduce production or deliveries, raise prices or renegotiate terms; our suppliers may become insolvent or cease trading; we may be unable to locate a suitable replacement supplier on acceptable terms or on a timely basis, or at all; and delays caused by supply issues may harm our reputation, frustrate our customers and cause them to turn to our competitors for future needs.

A significant portion of our cash and cash equivalents are held at a small number of banks.

A significant portion of our cash and cash equivalents is presently held at a small number of banks. Although our board has adopted a treasury policy requiring us to limit the amount of cash held by each banking group taking into account their credit ratings, we are subject to credit risk if any of these banks are unable to repay the balance in the applicable account or deliver our securities or if any bank should become bankrupt or otherwise insolvent. Any of the above events could have a material and adverse effect on our business, results of operations and financial condition.

Risks Related to Our Intellectual Property

We may not be able to adequately protect Epidiolex, nabiximols, our product candidates or our proprietary technology in the marketplace.

Our success will depend, in part, on our ability to obtain patents, protect our trade secrets and operate without infringing on the proprietary rights of others. We rely upon a combination of patents, plant variety rights, trade secret protection (i.e., know-how), and confidentiality agreements to protect the intellectual property of Epidiolex, nabiximols and our product candidates. The strengths of patents in the pharmaceutical field involve complex legal and scientific questions, and can be uncertain. Where appropriate, we seek patent protection for certain aspects of our products and technology. However, patent protection for naturally occurring compounds is exceedingly difficult to obtain, defend and enforce. Filing, prosecuting and defending patents throughout the world would be prohibitively expensive, so our policy is to look to patent technologies with commercial potential in jurisdictions with significant commercial opportunities. However, patent protection may not be available for some of the products or technology we are developing. If we must spend significant time and money protecting, defending or enforcing our patents, designing around patents held by others or licensing, potentially for large fees, patents or other proprietary rights held by others, our business, results of operations and financial condition may be harmed. We may not develop additional proprietary products that are patentable.

The patent positions of pharmaceutical products are complex and uncertain. The scope and extent of patent protection for Epidiolex, nabiximols and our product candidates are particularly uncertain. To date, our principal product candidates, including Epidiolex and nabiximols, have been based on specific formulations of certain previously known cannabinoids found in nature in the cannabis sativa plant. While we have sought patent protection, where appropriate, directed to, among other things, composition-of-matter for our specific formulations, their methods of use, and methods of manufacture, we do not have and will not be able to obtain composition of matter protection on these previously known cannabinoids per se. We anticipate that the products we develop in the future will continue to include or be based on the same or other naturally occurring compounds, as well as synthetic compounds we may discover. Although we have sought and expect to continue to seek patent protection for our product candidates, their methods of use, and methods of manufacture, any or all of them may not be subject to effective patent protection. For example, we are unable to obtain composition of matter patent protection for CBD, the active ingredient in Epidiolex, as it is a naturally occurring compound. If any of our products is approved and marketed for an indication for which we do not have an issued patent, our ability to use our patents to prevent a competitor from commercializing a non-branded version of our commercial products for that non-patented indication could be significantly impaired or even eliminated.

Publication of information related to Epidiolex, nabiximols and our product candidates by us or others may prevent us from obtaining or enforcing patents relating to these products and product candidates. Furthermore, others may independently develop similar products, may duplicate our products, or may design around our patent rights. In addition, any of our issued patents may be opposed and/or declared invalid or unenforceable. Two of our recently issued European patents, including our European patent claiming the use of CBD in the treatment of partial seizures, have received a notice of opposition, which may result in claims in these patents being narrowed or cancelled such that the scope of the opposed patent may not be as broad, or the opposed patent may be revoked in its entirety. In one of the opposition proceedings, the opponent failed to show the patent invalid. The other opposition

proceeding relating to CBD in the treatment of partial seizures resulted in an initial decision that is under appeal. One of our U.S. patents was involved in an Inter Partes Review proceeding before the USPTO that resulted in invalidation of certain but not all claims of that patent. If we fail to adequately protect our intellectual property, we may face competition from companies who attempt to create a generic product to compete with Epidiolex or Sativex. We may also face competition from companies who develop a substantially similar product to Epidiolex, Sativex or one of our other product candidates that is not covered by any of our patents.

Many companies have encountered significant problems in protecting, defending and enforcing intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property rights, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

If third parties claim that intellectual property used by us infringes upon their intellectual property, our operating profits could be adversely affected.

There is a substantial amount of litigation, both within and outside the U.S., involving patent and other intellectual property rights in the pharmaceutical industry. We may, from time to time, be notified of claims that we are infringing upon patents, trademarks, copyrights or other intellectual property rights owned by third parties, and we cannot provide assurances that other companies will not, in the future, pursue such infringement claims against us, our commercial partners or any third-party proprietary technologies we have licensed. If we were found to infringe upon a patent or other intellectual property right, or if we failed to obtain or renew a license under a patent or other intellectual property right from a third party, or if a third party that we were licensing technologies from was found to infringe upon a patent or other intellectual property rights of another third party, we may be required to pay damages, including damages of up to three times the damages found or assessed, if the infringement is found to be willful, suspend the manufacture of certain products or reengineer or rebrand our products, if feasible, or we may be unable to enter certain new product markets. Any such claims could also be expensive and time consuming to defend and divert management's attention and resources. Our competitive position could suffer as a result. In addition, if we have declined or failed to enter into a valid non-disclosure or assignment agreement for any reason, we may not own the invention or our intellectual property, and our products may not be adequately protected. Thus, we cannot guarantee that Epidiolex, Sativex or our other product candidates, or our commercialization thereof, does not and will not infringe any third party's intellectual property.

Risks Related to Controlled Substances

Controlled substance legislation differs between countries and legislation in certain countries may restrict or limit our ability to sell Epidiolex, nabiximols and our product candidates.

Most countries are parties to the Single Convention on Narcotic Drugs 1961, which governs international trade and domestic control of narcotic substances, including cannabis extracts. Countries may interpret and implement their treaty obligations in a way that creates a legal obstacle to our obtaining regulatory approval for Epidiolex, nabiximols and our other products in those countries. These countries may not be willing or able to amend or otherwise modify their laws and regulations to permit Epidiolex, nabiximols or our other products to be marketed, or achieving such amendments to the laws and regulations may take a prolonged period of time. In the case of countries with similar obstacles, we would be unable to market Epidiolex, nabiximols and our product candidates in countries in the near future or perhaps at all if the laws and regulations in those countries do not change.

Epidiolex is and the product candidates we are developing will be subject to U.S. controlled substance laws and regulations and failure to comply with these laws and regulations, or the cost of compliance with these laws and regulations, may adversely affect the results of our business operations, both during clinical development and post approval, and our financial condition.

Epidiolex, nabiximols and our product candidates we are developing contain controlled substances as defined in the federal Controlled Substances Act of 1970, or CSA. Controlled substances that are pharmaceutical products are subject to a high degree of regulation under the CSA, which establishes, among other things, certain registration, manufacturing quotas, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA classifies controlled substances into five schedules: Schedule I, II, III, IV or V substances. Schedule I substances by definition have a high potential for abuse, no currently "accepted medical use" in the U.S., lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the U.S. Pharmaceutical products approved for use in the U.S. which contain a controlled substance are listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse among such substances. Schedule I and II drugs are subject to the strictest controls under the CSA, including manufacturing and procurement quotas, security requirements and criteria for importation. In addition, dispensing of Schedule II drugs is further restricted. For example, they may not be refilled without a new prescription.

While cannabis is a Schedule I controlled substance, products approved for medical use in the U.S. that contain cannabis or cannabis extracts should be placed in Schedules II-V, since approval by the FDA satisfies the "accepted medical use" requirement. If and when any of our product candidates receive FDA approval, the DEA will make a scheduling determination. Having now been rescheduled into Schedule V, the manufacture, importation, exportation, domestic distribution, storage, sale and legitimate use of Epidiolex will still be subject to specific and potentially significant levels of regulation by the DEA. If any foreign regulatory authority determines that Epidiolex may have potential for abuse, or if FDA or DEA makes a similar determination for Sativex, it may require us to generate more clinical or other data than we currently anticipate to establish whether or to what extent the substance has an abuse potential, which could increase the cost and/or delay the launch of that product.

DEA registration and inspection of facilities. Facilities conducting research, manufacturing, distributing, importing or exporting, or dispensing controlled substances must be registered (licensed) to perform these activities and have the security, control, recordkeeping, reporting and inventory mechanisms required by the DEA to prevent drug loss and diversion. All these facilities must renew their registrations annually, except dispensing facilities, which must renew every three years. The DEA conducts periodic inspections of certain registered establishments that handle controlled substances. Obtaining and maintaining the necessary registrations may result in delay of the importation, manufacturing or distribution of Sativex and/or Epidiolex or other products. Furthermore, failure to maintain compliance with the CSA, particularly non-compliance resulting in loss or diversion, can result in regulatory action that could have a material adverse effect on our business, financial condition and results of operations. The DEA may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to restrict, suspend or revoke those registrations. In certain circumstances, violations could lead to criminal proceedings.

State-controlled substances laws. Individual states have also established controlled substance laws and regulations. Though state-controlled substances laws often mirror federal law, because the states are separate jurisdictions, they may separately schedule Epidiolex or our product candidates as well. We or our partners must also obtain separate state registrations, permits or licenses in order to be able to obtain, handle, and distribute controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions by the states in addition to those from the DEA or otherwise arising under federal law.

Clinical trials. Because our products are controlled substances in the U.S., to conduct clinical trials in the U.S., each of our research sites must submit a research protocol to the DEA and obtain and maintain a DEA researcher registration that will allow those sites to handle and dispense our products and to obtain product from our importer. If the DEA delays or denies the grant of a research registration to one or more research sites, the clinical trial could be significantly delayed, and we could lose clinical trial sites. The importer for the clinical trials must also obtain an importer registration and an import permit for each import. We do not currently conduct any manufacturing or repackaging/relabeling of Sativex or its active ingredients (i.e., the cannabis extract) in the U.S.

Importation. If one of our product candidates is approved and classified as a Schedule II or III substance, an importer can import for commercial purposes if it obtains an importer registration and files an application for an import permit for each import. The DEA provides annual assessments/estimates to the International Narcotics Control Board which guides the DEA in the amounts of controlled substances that the DEA authorizes to be imported. The failure to identify an importer or obtain the necessary import authority, including specific quantities, could affect product availability and have a material adverse effect on our business, results of operations and financial condition. In addition, an application for a Schedule II importer registration must be published in the Federal Register, and there is a waiting period for third party comments to be submitted. It is always possible that adverse comments may delay the grant of an importer registration.

If one of our product candidates is approved and classified as a Schedule II controlled substance, federal law may impose additional restrictions on importation for commercial purposes.

Manufacture in the U.S. If, because of a Schedule II classification or voluntarily, we were to conduct manufacturing or repackaging/relabeling in the U.S., our contract manufacturers would be subject to the DEA's annual manufacturing and procurement quota requirements. Additionally, regardless of the scheduling of Epidiolex and nabiximols, cannabis and the BDSs comprising the active ingredient in the final dosage form are currently Schedule I controlled substances and would be subject to such quotas as these substances could remain listed on Schedule I. The annual quota allocated to us or our contract manufacturers for the active ingredients in our products may not be sufficient to complete clinical trials or meet commercial demand. Consequently, any delay or refusal by the DEA in establishing our, or our contract manufacturers', procurement and/or production quota for controlled substances could delay or stop our clinical trials or product launches, which could have a material adverse effect on our business, financial position and results of operations.

Distribution in the U.S. If any of our product candidates is scheduled as Schedule II or III, we would also need to identify wholesale distributors with the appropriate DEA and state registrations and authority to distribute the product to pharmacies and other health care providers. We would need to identify distributors to distribute the product to pharmacies; these distributors would need to obtain Schedule II or III distribution registrations. The failure to obtain, or delay in obtaining, or the loss any of those registrations could result in increased costs to us. If any of our product candidates is a Schedule II drug, pharmacies would have to maintain enhanced

security with alarms and monitoring systems and they must adhere to recordkeeping and inventory requirements. This may discourage some pharmacies from carrying either or both of these products. Furthermore, state and federal enforcement actions, regulatory requirements, and legislation intended to reduce prescription drug abuse, such as the requirement that physicians consult a state prescription drug monitoring program may make physicians less willing to prescribe, and pharmacies to dispense, Schedule II products.

The legalization and use of medical and recreational marijuana in the U.S. and elsewhere may impact our business.

There is a substantial amount of change occurring in the U.S. regarding the use of medical and recreational marijuana products. While federal law prohibits the sale and distribution of most marijuana products not approved or authorized by the FDA, at least 33 jurisdictions and the District of Columbia have enacted state laws to enable possession and use of marijuana for medical purposes, and at least ten jurisdictions for recreational purposes. Under the U.S. Farm Bill, enacted in late 2018, certain extracts and other material derived from certain marijuana plants are now descheduled from the CSA. Although the marketing of such products as a food, dietary supplement, or for medical purposes remains subject to FDA requirements and is not currently permitted, the FDA continues to evaluate regulatory pathways to permit CBD in conventional foods and dietary supplements. In addition, Congress held a hearing in January 2020 on several reform proposals that could result in broader legalization of marijuana products. Although our business is quite distinct from that of unapproved marijuana and dietary supplement companies, future legislation or FDA action authorizing the sale, distribution, use, and insurance reimbursement of non-FDA approved marijuana products could affect our business.

Risks Related to Ownership of Our ADSs

The market price of our ADSs may be volatile.

Many factors may have a material adverse effect on the market price of the ADSs, including, but not limited to:

- the loss of any of our key scientific or management personnel;
- announcements of the failure to obtain regulatory approvals or receipt of a complete response letter from the FDA;
- announcements of restricted label indications or patient populations, or changes or delays in regulatory review processes;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities, including actions with respect to any regulatory exclusivities for our drugs and our drug candidates;
- changes or developments in laws or regulations applicable to Epidiolex, Sativex and our other product candidates;
- any adverse changes to our relationship with licensors, manufacturers or suppliers;
- the failure of our testing and clinical trials;
- the failure to retain our existing, or obtain new, collaboration partners;
- announcements concerning our competitors or the pharmaceutical industry in general;
- the achievement of expected product sales and profitability;
- the failure to obtain reimbursements for our products or price reductions;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our operating results;
- our cash position;
- changes in financial estimates or recommendations by securities analysts;
- potential acquisitions;

- the trading volume of ADSs on the Nasdaq Global Market;
- sales of our ADSs or ordinary shares by us, our executive officers and directors or our shareholders in the future;
- the impact on the financial markets or otherwise of the expected withdrawal of the United Kingdom from the European Union;
- natural disasters and political and economic instability, including wars, terrorism, political unrest, results of certain elections and votes, actual or threatened public health emergencies and outbreak of disease (including for example, the recent coronavirus outbreak), boycotts, adoption or expansion of government trade restrictions, and other business restrictions;
- general economic and market conditions and overall fluctuations in the U.S. equity markets; and
- changes in accounting principles.

In addition, the stock market in general, and Nasdaq in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of individual companies. The market for equity securities in pharmaceutical companies, in particular, has at various times experienced extreme volatility. Broad market and industry factors may negatively affect the market price of our ADSs, regardless of our actual operating performance.

In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation often has been instituted against that company.

Our largest shareholder owns a significant percentage of our share capital and voting rights of the Company.

As of December 31, 2019, Capital Research Global Investors, a division of Capital Research and Management Company, held approximately 11.7% of our issued share capital, accounting for approximately 11.7% of the voting rights of the Company, and Capital World Investors, also a division of Capital Research and Management Company, held approximately 3.5% of our issued share capital, accounting for approximately 3.5% of the voting rights of the Company. An aggregate of 15.2% of our issued share capital, accounting for approximately 15.2% of the voting rights of the Company, is collectively held by these Capital Research and Management Company divisions. To the extent these divisions of Capital Research and Management Company continue to collectively hold a large percentage of our share capital and voting rights, they will remain in a position to exert greater influence in the appointment of our directors and officers and in other corporate actions that require shareholders' approval.

Substantial future sales of our ADSs in the public market, or the perception that these sales could occur, could cause the price of the ADSs to decline.

Sales of our ADSs in the public market, or the perception that these sales could occur, could cause the market price of the ADSs to decline. The ordinary shares held by our directors, including our officers, are available for sale in the form of ADSs and are not subject to contractual and legal restrictions on resale. If any of our large shareholders or members of our management team seek to sell substantial amounts of our ADSs, particularly if these sales are in a rapid or disorderly manner, or other investors perceive that these sales could occur, the market price of our ADSs could decrease significantly.

U.S. investors may have difficulty enforcing civil liabilities against our Company, our directors or members of senior management and the experts named in this Annual Report.

We are incorporated under the laws of England and Wales, and our subsidiaries are incorporated in various jurisdictions, including foreign jurisdictions. A number of the officers and directors of the Company and each of our subsidiaries and some of the experts named in this Annual Report are non-residents of the United States, and all or a substantial portion of the assets of such persons are located outside the United States. Mayer Brown International LLP, our English solicitors, advised us that there is doubt as to whether English courts would enforce certain civil liabilities under U.S. securities laws in original actions or judgments of U.S. courts based upon these civil liability provisions. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in the United Kingdom. An award for monetary damages under the U.S. securities laws would be considered punitive if it does not seek to compensate the claimant for loss or damage suffered and is intended to punish the defendant. The enforceability of any judgment in the United Kingdom will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and the United Kingdom do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters

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

We are incorporated under English law. The rights of holders of ordinary shares, and therefore certain of the rights of shareholders, are governed by English law, including the provisions of the Companies Act 2006, and by our substituted articles of association (Articles of Association). These rights differ in certain respects from the rights of shareholders in typical U.S. corporations. Certain differences between the provisions of the Companies Act 2006 applicable to us and the Delaware General Corporation Law, or DGCL, relating to shareholders' rights and protections include, but are not limited to, the following.

- Under English law and our Articles of Association, each shareholder present at a meeting has only one vote unless demand is made for a vote on a poll, in which case each holder gets one vote per share owned. Under U.S. law, each shareholder typically is entitled to one vote per share at all meetings. However, the voting rights of our shares are also governed by the provisions of a deposit agreement with our depositary bank.

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

- In the U.K., takeovers may be structured as takeover offers or as schemes of arrangement. Under English law, a bidder seeking to acquire us by means of a takeover offer would need to make an offer for all of our outstanding ordinary shares or ADSs. If acceptances are not received for 90% or more of the ordinary shares or ADSs under the offer, under English law, the bidder cannot complete a "squeeze out" to obtain 100% control of us. Accordingly, acceptances of 90% of our outstanding ordinary shares or ADSs will likely be a condition in any takeover offer to acquire us, not 50% as is more common for corporations organized under Delaware law. By contrast, a scheme of arrangement, the successful completion of which would result in a bidder obtaining 100% control of us, requires the approval of a majority of shareholders voting at the meeting and representing 75% of the ordinary shares voting for approval.

- Under English law, certain matters require the approval by special resolution. To be passed, a special resolution requires (on a show of hands) a majority of not less than 75% of the votes cast by those entitled to vote or (on a poll) a majority of not less than 75% of the total voting rights of the members who (being entitled to do so) vote in person or by proxy on the resolution. The matters requiring approval by special resolution include amendments to the Articles of Association. Under U.S. law, generally only majority shareholder approval is required to amend the certificate of incorporation or to approve other significant transactions.

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

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

The U.K. City Code on Takeovers and Mergers, or the Takeover Code, which is issued and administered by the U.K. Panel on Takeovers and Mergers, of the Takeover Panel, provides a framework within which takeovers of companies subject to it are conducted, including, in particular, certain rules in respect of mandatory offers. In March 2018, the Takeover Panel confirmed that, based on our current circumstances, we are not subject to the Takeover Code. As a result, our shareholders are not entitled to the benefit of certain takeover offer protections provided under the Takeover Code. We believe that this position is unlikely to change at any time in the near future but, in accordance with good practice, we will review the situation on a regular basis and consult with the Takeover Panel if there is any change in our circumstances on this subject.

We may be classified as a passive foreign investment company, or PFIC, in any taxable year and U.S. holders of our ADSs could be subject to adverse U.S. federal income tax consequences.

The rules governing PFICs can have adverse effects for U.S. federal income tax purposes. The tests for determining PFIC status for a taxable year depend upon the relative values of certain categories of assets and the relative amounts of certain kinds of income. The determination of whether we are a PFIC depends on the particular facts and circumstances (such as the valuation of our assets, including goodwill and other intangible assets) and may also be affected by the application of the PFIC rules, which are subject to differing interpretations. Based on our estimated gross income, the average value of our assets, including goodwill and the nature of our active business, we do not believe that we were classified as a PFIC for U.S. federal income tax purposes for the taxable year ending December 31, 2019. There can be no assurance, however, that we will not be considered to be a PFIC for this taxable year or any particular year in the future because PFIC status is factual in nature, depends upon factors not wholly within our control, generally cannot be determined until the close of the taxable year in question and is determined annually.

If we are a PFIC, U.S. holders of our ADSs would be subject to adverse U.S. federal income tax consequences, such as ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements under U.S. federal income tax laws and regulations. A U.S. holder of our ADSs may be able to mitigate some of the adverse U.S. federal income tax consequences described above with respect to owning ADSs if we are classified as a PFIC, provided that such U.S. investor is eligible to make, and validly makes, a “mark-to-market” election. In certain circumstances a U.S. holder can make a “qualified electing fund” election to mitigate some of the adverse tax consequences described with respect to an ownership interest in a PFIC by including in income its share of the PFIC’s income on a current basis. However, we do not currently intend to prepare or provide the information that would enable a U.S. holder to make a qualified electing fund election.

Investors should consult their own tax advisors regarding all aspects of the application of the PFIC rules to our ordinary shares.

Item 1B. Unresolved Staff Comments

There are no written comments from the staff of the SEC which remain unresolved before the end of the fiscal year to which the Annual Report relates.

Item 2. Properties

Our operations are conducted in leased facilities located in the United Kingdom and the United States. In addition to our leased administrative, research and manufacturing facilities, we also have dedicated growing facilities operated by contract partners. The following table provides a summary of our significant properties as of December 31, 2019:

Type	Location	Size (sq. ft.)	Lease / Contract Expiration
Administrative office	London, United Kingdom	6,950	2028
Administrative office	Cambridge, United Kingdom	16,036	2021-2023
Administrative office	Carlsbad, United States	62,714	2023-2025
Research and manufacturing	Southern United Kingdom	138,547	2022-2033
Growing facility	Eastern United Kingdom	1,960,000	2021
Growing facility	Northern United Kingdom	914,760	2020
Growing facility	Southern United Kingdom	328,837	2020-2028

We believe that our office, research and manufacturing facilities are sufficient to meet our current needs. We are not aware of any environmental issues that may affect our utilization of our property.

Item 3. Legal Proceedings

As of December 31, 2019, we were not a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Our ordinary shares, par value £0.001 per share, are not publicly traded. Our American Depositary Shares (ADSs) each represent twelve ordinary shares of GW Pharmaceuticals plc. An ADS may be evidenced by an American Depositary Receipt (ADR) issued by Citibank., N.A. as depositary, and is listed on the Nasdaq Global Market under the symbol "GWPH" since May 1, 2013.

Prior to that date, there was no public trading market for our ADSs. Our ordinary shares were traded on the Alternative Investment Market, or AIM, a market operated by London Stock Exchange plc, under the symbol GWP between June 28, 2001 and December 5, 2016.

Holders of Ordinary Shares and ADSs

As of December 31, 2019, there were approximately 1,001 holders of record of our ordinary shares and 380 holders of record of our ADSs. The closing sale price per ADS on the Nasdaq Global Market on February 21, 2020 was $125.69.

Dividends

Since our inception, we have not declared or paid any dividends on our ordinary shares. We intend to retain any earnings for use in our business and do not currently intend to pay dividends on our ordinary shares.

The payment of dividends by us is governed by English law. The declaration and payment of any future dividends will be at the discretion of our board of directors and will depend upon our results of operations, cash requirements, financial condition, contractual restrictions, restrictions imposed by our indebtedness, any future debt agreements or applicable laws and other factors that our board of directors may deem relevant.

Information about Our Equity Compensation Plans

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

Performance Graph

The following graph shows the cumulative total shareholder return of an investment of $100 in cash at market close over the five-year period ending December 31, 2019 for (1) our ADSs, (2) the Nasdaq Biotechnology Index and (3) the Nasdaq Composite Index (U.S.).

This performance graph shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or incorporated by reference into any of our filings under the U.S. Securities Act of 1933, as amended (Securities Act) or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Recent Sales of Unregistered Securities

We did not sell any unregistered securities during the year ended December 31, 2019.

Item 6. Selected Financial Data

The following table sets forth our consolidated financial data. The selected consolidated financial data as of December 31, 2019 and 2018 and for the year ended December 31, 2019, three months ended December 31, 2018, and years ended September 30, 2018 and 2017, presented in this table have been derived from our audited consolidated financial statements and related notes included elsewhere in this Annual Report. The information set forth below is not necessarily indicative of our results of future operations and should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the financial statements and notes thereto appearing elsewhere in this Annual Report on Form 10-K.

	Year Ended December 31,	Three Months Ended December 31,	Years Ended September 30,		
	2019	2018	2018	2017	2016
	(in thousands, except per share amounts)				
Consolidated Statement of Operations Data:					
Revenues:					
Product net sales	$ 310,331	$ 6,617	$ 10,469	$ 7,957	$ 7,317
Other revenue	1,001	37	2,268	672	5,413
Total revenues	311,332	$ 6,654	12,737	8,629	12,730
Operating expenses:					
Cost of product sales	27,199	1,829	5,986	4,521	3,820
Research and development	142,678	29,086	153,736	112,249	104,375
Selling, general and administrative	259,880	49,083	141,818	58,020	33,188
Total operating expenses	429,757	79,998	301,540	174,790	141,383
Loss from operations	(118,425)	(73,344)	(288,803)	(166,161)	(128,653)
Interest income	8,464	2,449	3,645	2,063	611
Interest expense	(1,087)	(295)	(1,249)	(951)	(244)
Other income	104,117	—	—	—	—
Foreign exchange (loss) gain	(2,272)	(982)	(4,963)	(6,442)	35,897
Loss before income taxes	(9,203)	(72,172)	(291,370)	(171,491)	(92,389)
Income tax (benefit) expense	(184)	(266)	3,797	(1,032)	(693)
Net loss	$ (9,019)	$ (71,906)	$ (295,167)	$ (170,459)	$ (91,696)
Net loss per common share, basic and diluted	$ (0.02)	$ (0.20)	$ (0.88)	$ (0.56)	$ (0.34)
Weighted average common shares outstanding, basic and diluted	371,580	366,458	333,936	305,826	272,165

	December 31,		September 30,		
	2019	2018	2018	2017	2016
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 536,933	$ 591,497	$ 354,913	$ 322,154	$ 483,445
Working capital	582,075	580,406	332,042	319,673	480,742
Total assets	882,249	756,068	490,535	442,922	583,315
Total liabilities	156,215	81,988	75,376	62,099	57,642
Total stockholders' equity	726,034	674,080	415,159	380,823	525,673

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

The following discussion contains management's discussion and analysis of our financial condition and results of operations and should be read together with "Selected Financial Data" and the historical consolidated financial statements and the notes thereto included in "Financial Statements and Supplementary Data". This discussion contains forward-looking statements that reflect our plans, estimates and beliefs and involve numerous risks and uncertainties, including but not limited to those described in the "Risk Factors" section of this Annual Report. Actual results may differ materially from those contained in any forward-looking statements. You should carefully read "Information Regarding Forward-Looking Statements" and "Risk Factors."

Overview

GW Pharmaceuticals plc was founded in 1998 and is a public limited company incorporated under the laws of England and Wales. Our ordinary shares were admitted to trading on the Alternative Investment Market, or AIM, a market operated by London Stock Exchange plc, under the symbol GWP on June 28, 2001. On May 1, 2013, we completed our initial public offering of ADSs, on the Nasdaq Global Market. Our ADSs are traded under the symbol GWPH. We cancelled the admission of our ordinary shares to trading on AIM on December 5, 2016 and our shares are now traded exclusively on Nasdaq.

We are a biopharmaceutical company focused on discovering, developing and commercializing novel therapeutics from our proprietary cannabinoid product platform in a broad range of disease areas. In over 20 years of operations, we have established a world leading position in the science, development and commercialization of plant-derived cannabinoid therapeutics through our proven drug discovery and development processes, our intellectual property portfolio, regulatory, manufacturing, and commercial expertise.

Our lead cannabinoid product is Epidiolex, a pharmaceutical formulation of cannabidiol for which we retain global commercial rights. Epidiolex is approved in the United States for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS) and Dravet syndrome, in patients two years of age and older. LGS and Dravet syndrome are severe childhood-onset, drug-resistant epilepsy syndromes. We launched Epidiolex in the United States in November 2018. In September 2019, we received approval from the European Commission for Epidyolex (the trade name in Europe for Epidiolex) for use as adjunctive therapy of seizures associated with LGS or Dravet syndrome, in conjunction with clobazam, for patients two years of age and older. We have launched Epidyolex in Germany and the U.K. and are planning launches in France, Italy and Spain during 2020.

We continue to develop Epidiolex for additional indications. In May 2019, we announced positive results from a Phase 3 trial in the use of Epidiolex to treat seizures associated with Tuberous Sclerosis Complex, or TSC, a rare genetic disorder that causes non-malignant tumors to form in many different organs that affects approximately 50,000 individuals in the United States and one million worldwide. On February 3, 2020, we announced that we had submitted a supplemental New Drug Application to the U.S. Food and Drug Administration, or FDA, to expand the Epidiolex label to include the treatment of seizures associated with TSC. We expect to file for supplemental approval for the TSC indication in Europe in the first quarter of 2020. We have received Orphan Drug Designation from the FDA and the Committee for Orphan Medical Products for TSC (we previously received the same designations for Dravet syndrome and LGS).

We have begun recruiting patients for a pivotal trial of Epidiolex in the treatment of Rett syndrome, a rare, non-inherited neurodevelopmental disorder affecting approximately one in 10,000 to 15,000 live female births. This trial focuses on the behavioral abnormalities associated with the disorder.

We have a deep pipeline of additional cannabinoid product candidates that includes compounds in Phase 1, Phase 2, and Phase 3 trials. Our most advanced pipeline asset is nabiximols, for which we expect to commence a pivotal clinical program in the first half of 2020 in the treatment of spasticity due to multiple sclerosis. We anticipate commercializing nabiximols in the U.S. using our in-house commercial organization. Nabiximols is already approved in over 25 countries outside the United States for the treatment of spasticity due to multiple sclerosis under the brand name Sativex. We are advancing plans to commence clinical programs for nabiximols in 2020 in spasticity due to spinal cord injury and post-traumatic stress disorder.

In addition to nabiximols, our pipeline includes cannabinoid product candidates for schizophrenia, autism spectrum disorder, and Neonatal Hypoxic Ischemic Encephalopathy.

Change of Fiscal Year

We changed our fiscal year end to December 31 from September 30, effective December 31, 2018. This annual report is for the year ended December 31, 2019.

Critical Accounting Policies and Estimates

Our consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States or U.S. GAAP. These accounting principles require us to make certain estimates, judgments and assumptions that affect the reported amounts of assets and liabilities as of the date of the financial statements, as well as the reported amounts of revenues and expenses during the periods presented. We believe that the estimates, judgments and assumptions are reasonable based upon information available to us at the time that these estimates, judgments and assumptions are made. To the extent there are material differences between these estimates, judgments or assumptions and actual results, our financial statements will be affected. Historically, revisions to our estimates have not resulted in a material change to our financial statements. The significant accounting estimates that we believe are important to aid in fully understanding and evaluating our reported financial results include the following:

Revenue recognition

We recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that are within the scope of Accounting Standards Codification (ASC) Topic 606, Revenue from Contracts with Customers (Topic 606), we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only applies the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract and determine those that are performance obligations and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Revenue for our product sales has not been adjusted for the effects of a financing component as we expect, at contract inception, that the period between when we transfer control of the product and when we receive payment will be one year or less. Product shipping and handling costs are included in cost of product sales.

Epidiolex

Epidiolex was approved by the FDA in June 2018. That approval became effective when the United States Drug Enforcement Agency (DEA) took action to change the classification of Epidiolex from a Schedule I controlled substance to a Schedule V controlled substance, thereby allowing Epidiolex to be prescribed and distributed in the United States. On November 1, 2018, we launched sales of Epidiolex to specialty pharmacies (SPs) and specialty distributors (SDs). We recognize revenue from product sales upon receipt of product at the SPs and SDs, the date at which the control is transferred, net of the following allowances which are reflected either as a reduction to the related account receivable or as an accrued liability, depending on how the allowance is settled:

Distribution Fees: Distribution fees include distribution service fees paid to the SPs and SDs based on a contractually fixed percentage of the wholesale acquisition cost (WAC), and prompt payment discounts. Distribution fees are recorded as an offset to revenue based on contractual terms at the time revenue from the sale is recognized.

Rebates: Allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program and the Medicare Part D prescription drug benefit, and contractual rebates with commercial payers. Rebates are amounts owed after the final dispensing of the product to a benefit plan participant and are based upon contractual agreements or statutory requirements. The allowance for rebates is based on contracted or statutory discount rates and expected utilization by benefit plan participants. Our estimates for expected utilization of rebates is based on utilization data received from the SPs since product launch. Rebates are generally invoiced and paid in arrears so that the accrual balance consists of an estimate of the amount expected to be incurred for the current quarter’s activity, plus an accrual balance for prior quarters’ unpaid rebates. If actual future rebates vary from estimates, we may need to adjust prior period accruals, which would affect revenue in the period of adjustment.

Chargebacks: Chargebacks are discounts and fees that relate to contracts with government and other entities purchasing from the SDs at a discounted price. The SDs charge back to us the difference between the price initially paid by the SDs and the discounted price paid to the SDs by these entities. We also incur group purchasing organization fees for transactions through certain purchasing organizations. We estimate sales with these entities and accrue for anticipated chargebacks and organization fees, based on the applicable contractual terms. If actual future chargebacks vary from these estimates, we may need to adjust prior period accruals, which would affect revenue in the period of adjustment.

Co-Payment Assistance: We offer co-payment assistance to commercially insured patients meeting certain eligibility requirements. Co-payment assistance is accrued for based on actual program participation and estimates of program redemption using data provided by third-party administrators.

Product Returns: Consistent with industry practice, we offer the SPs and SDs limited product return rights for damages, shipment errors, and expiring product, provided that the return is within a specified period around the product expiration date as set forth in the applicable individual distribution agreement. We do not allow product returns for product that has been dispensed to a patient. As we receive inventory reports from the SPs and SDs and have the ability to control the amount of product that is sold to the SPs and SDs, we are able to make a reasonable estimate of future potential product returns based on this on-hand channel inventory data and sell-through data obtained from the SPs and SDs. In arriving at its estimate, we also considers historical product returns, the underlying product demand, and industry data specific to the specialty pharmaceutical distribution industry.

On September 23, 2019, we announced that the European Commission approved the marketing authorization for Epidyolex (the trade name in Europe for Epidiolex) for use as adjunctive therapy of seizures associated with Lennox-Gastaut syndrome, or LGS, or Dravet syndrome, in conjunction with clobazam, for patients two years of age and older. We recognize revenue from product sales in Europe upon delivery of the product, which is the point at which control of the goods is transferred to the customer. We recognize revenue net of standard discounts and allowances, which are reflected as accrued liabilities.

We also sell Epidiolex in certain markets outside of the United States under early access programs that enable patients to receive the product prior to regulatory approval. Revenue under early access programs is generally recognized when the product is delivered.

Sativex

Our product sales of Sativex, sold outside of the United States for the treatment of spasticity due to multiple sclerosis, or MS, are made pursuant to license agreements with commercial partners. Under these license agreements, we sell fully labeled Sativex vials to our commercial partners for a contractually agreed price, which is generally based on percentages of the commercial partners' in-market net selling price charged to end customers. Product net sales revenue related to Sativex shipments to commercial license partners is recognized when shipped, at which point the customer obtains control of the product. We commercialize Sativex in Australia and New Zealand through a consignment relationship with a local distributor. Product net sales revenues related to Sativex sales in Australia and New Zealand are recognized when the product is sold through to the end customer.

The Sativex license agreements contain provisions for us to earn future variable consideration in the form of regulatory milestone payments, sales-based milestone payments, and royalty payments. We have no further performance obligations related to the regulatory milestone payments and these amounts will be recognized in accordance with Topic 606 when receipt of these payments becomes probable and there is no significant risk of revenue reversal. Revenue related to the sales-based milestone payments and product royalty payments are subject to the sales-based royalty exception under Topic 606 and will be recognized when the underlying sales are made.

Share-Based Compensation

We recognize share-based compensation expense for grants of stock options under our long-term incentive plans to employees and non-employee members of the board of directors based on the grant-date fair value of those awards. The grant-date fair value of an award is generally recognized as compensation expense over the award's requisite service period. Expense related to awards with graded vesting is generally recognized over the vesting period using the accelerated attribution method.

We use the Black-Scholes model to compute the estimated fair value of stock option awards. Using this model, fair value is calculated based on assumptions with respect to (i) expected volatility of the Company's ADS price, (ii) the periods of time over which employees and members of the board of directors are expected to hold their options prior to exercise (expected lives), (iii) expected dividend yield on the ordinary shares, and (iv) risk-free interest rates. Share-based compensation expense also includes an estimate, which is made at the time of grant, of the number of awards that are expected to be forfeited. This estimate is revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Inventory

Inventory is stated at the lower of cost or estimated net realizable value. We use a combination of standard and actual costing methodologies to determine the cost basis for our inventories, which approximates actual cost. Inventory is valued on a first-in, first-out basis. We reduce our inventory to net realizable value for potentially excess, dated or obsolete inventory based on an analysis of forecasted demand compared to quantities on hand, as well as product shelf life.

Our inventory production process includes the cultivation of botanical raw material. Because of the duration of the cultivation process, a substantial portion of our inventory will not be sold within one year. Consistent with the practice in other industries that cultivate botanical raw materials, all inventory is classified as a current asset.

We capitalize inventory costs associated with our products upon regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed. Prior to FDA approval of Epidiolex, all costs related to the manufacturing of Epidiolex were charged to research and development expense in the period incurred.

U.K. Research and Development (R&D) Tax and Expenditure Credits

Prior to September 30, 2017, we benefited from the U.K. Small and Medium-sized Enterprise R&D Tax Credit scheme, or the SME scheme, under which we were able to obtain a refundable credit of up to 33.4% of eligible research and development expenses incurred by our U.K. domiciled entities. Eligible expenses generally include employment costs for research staff, consumables and certain internal overhead costs incurred as part of research projects. Additionally, subcontracted research expenses are eligible for a cash rebate of up to approximately 21.68%. Due to the increase in the size of our employee workforce in the U.K. and our annual net revenues, beginning in October 1, 2017 we are subject to the U.K. R&D Expenditure Credit scheme, or the RDEC scheme, available to larger companies, which has a significantly lower credit than the SME scheme. The majority of our pipeline research, clinical trials management and the Epidiolex and Sativex chemistry and manufacturing controls development activities, which are generally carried out by a subsidiary in the U.K., are eligible for inclusion under the SME and RDEC schemes. Reimbursable credits accrued under these schemes reduce our research and development expense in the period that the qualifying expenses are incurred.

We estimate a benefit under the RDEC scheme of $4.0 million for the year ended December 31, 2019, $0.8 million for the three months ended December 31, 2018, and a $4.3 million benefit for the year ended September 30, 2018. We develop estimates at each reporting date for the amount of the reimbursable research and development tax and expense credits and ultimately make reimbursement claims from Her Majesty's Revenue and Customs, or HMRC, as part of the annual U.K. tax return. Such claims are complex and require management to interpret and apply U.K. research and development tax legislation to our specific circumstances which requires the use of certain assumptions in estimating the portion of current year research costs that are eligible for the claim. If actual reimbursements differ from our estimates, adjustments to prior period accruals would affect the amount of research and development expense in the period of the adjustment.

Deferred Income Taxes

Deferred tax is accounted for using the asset and liability method that requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the financial statement carrying amount and the tax bases of assets and liabilities at the applicable tax rates. As of December 31, 2019, we have deferred tax assets of $134.2 million, offset by deferred tax liabilities of $1.6 million and a valuation allowance of $114.5 million.

A valuation allowance is provided when it is more-likely-than-not that some portion or all of the deferred tax assets will not be realized. Future realization of the tax benefit of a deferred tax asset depends on the existence of sufficient taxable income of the appropriate character (for example, ordinary income or capital gain) within the carryback or carryforward period available under the tax law. We consider the following possible sources of taxable income when assessing whether there is sufficient taxable income to realize a tax benefit for deductible temporary differences and carryforwards:

- future reversals of existing taxable temporary differences;
- future taxable income exclusive of reversing temporary differences and carryforwards;
- taxable income in prior carryback year(s) if carryback is permitted under the tax law; and
- tax-planning strategies.

We consider both positive and negative evidence regarding realization of the deferred tax assets and the subjectivity of this evidence. This assessment includes estimating future taxable income, scheduling reversals of temporary differences, evaluating expectations of future profitability, determining refund potential in the event of net operating loss carrybacks, and evaluating potential tax-planning strategies.

We have generated losses in the United Kingdom since inception and expect to generate tax losses next year and therefore the deferred tax assets arising in the United Kingdom do not meet the more-likely-than-not of being realized threshold. Accordingly, there continues to be a full valuation allowance against deferred taxes in the U.K.

Our U.S. subsidiary, Greenwich Biosciences, Inc., is currently profitable and incurs a U.S. tax liability on taxable profits earned in the United States. Due to the commercialization of Epidiolex in the United States and income related to service agreements between our U.S. and U.K. operating subsidiaries, our U.S. subsidiary is forecast to continue to generate taxable income in future periods. In determining whether the deferred tax asset is more-likely-than-not of being realized, we have taken into account the history of taxable profits, the forecast of future taxable income, including whether future originating temporary deductible differences are likely to be realized, and the reversal of temporary taxable deductions. We have determined that the deferred tax for Greenwich Biosciences, Inc. is more-likely-than-not to be realized and therefore have no valuation allowance against the U.S. deferred tax balances.

Forecasting U.S. taxable income is by nature subject to known and unknown risks, uncertainties, assumptions and other factors that could negatively impact our ability to realize the value of our deferred tax assets. These risks include our ability to successfully grow our product sales of Epidiolex in the U.S. market and source future product development work to the U.S. subsidiary. If we determine in the future that an amount of our U.S. deferred tax assets fail to meet the more-likely-than-not to be realizable threshold, there will be a negative impact on our provision for income taxes and the amount of deferred tax assets recognized in our consolidated balance sheet. The amount of deferred taxes for our U.S. subsidiary included in our consolidated balance sheets is $18.1 million and $8.7 million as of December 31, 2019 and 2018, respectively.

Recent Accounting Pronouncements

See Item 15 of Part IV, “Notes to Consolidated Financial Statements—Note 2—Summary of Significant Accounting Policies.”

Results of Operations

The following table summarizes the results of our operations for the years ended December 31, 2019 and 2018. The income statement data for the year ended December 31, 2019 are derived from the audited consolidated financial statements included in Item 6 – Selected Financial Data. The income statement data for the year ended December 31, 2018 are derived from our unaudited consolidated financial statements for that period.

	Year Ended December 31,		
	2019	2018	Increase/Decrease
		(in thousands)	
Consolidated Statement of Operations Data:			
Revenues:			
Product net sales	$ 310,331	$ 14,866	$ 295,465
Other revenue	1,001	533	468
Total revenues	311,332	15,399	295,933
Operating expenses:			
Cost of product sales	27,199	6,644	20,555
Research and development	142,678	146,627	(3,949)
Selling, general and administrative	259,880	165,727	94,153
Total operating expenses	429,757	318,998	110,759
Loss from operations	(118,425)	(303,599)	185,174
Interest income	8,464	5,490	2,974
Interest expense	(1,087)	(1,230)	143
Other income	104,117	—	104,117
Foreign exchange (loss) gain	(2,272)	(6,105)	3,833
Loss before income taxes	(9,203)	(305,444)	296,241
Income tax (benefit) expense	(184)	(187)	3
Net loss	$ (9,019)	$ (305,257)	$ 296,238

The following table summarizes the results of our operations for the three months ended December 31, 2018 and 2017. The income statement data for the three months ended December 31, 2018 are derived from the audited consolidated financial statements included in Item 6 – Selected Financial Data. The income statement data for the three months ended December 31, 2017 are derived from our unaudited consolidated financial statements for that period.

	Three Months Ended December 31,		
	2018	2017	Increase/Decrease
	(in thousands)		
Consolidated Statement of Operations Data:			
Revenues:			
Product net sales	$ 6,617	$ 2,220	$ 4,397
Other revenue	37	1,772	(1,735)
Total revenues	6,654	3,992	2,662
Operating expenses:			
Cost of product sales	1,829	1,171	658
Research and development	29,086	36,195	(7,109)
Selling, general and administrative	49,083	25,174	23,909
Total operating expenses	79,998	62,540	17,458
Loss from operations	(73,344)	(58,548)	(14,796)
Interest income	2,449	604	1,845
Interest expense	(295)	(314)	19
Foreign exchange (loss) gain	(982)	160	(1,142)
Loss before income taxes	(72,172)	(58,098)	(14,074)
Income tax (benefit) expense	(266)	3,718	(3,984)
Net loss	$ (71,906)	$ (61,816)	$ (10,090)

The following table summarizes the results of our operations for the years ended September 30, 2018 and 2017:

	Years Ended September 30,		
	2018	2017	Increase/Decrease
	(in thousands)		
Consolidated Statement of Operations Data:			
Revenues:			
Product net sales	$ 10,469	$ 7,957	$ 2,512
Other revenue	2,268	672	1,596
Total revenues	12,737	8,629	4,108
Operating expenses:			
Cost of product sales	5,986	4,521	1,465
Research and development	153,736	112,249	41,487
Selling, general and administrative	141,818	58,020	83,798
Total operating expenses	301,540	174,790	126,750
Loss from operations	(288,803)	(166,161)	(122,642)
Interest income	3,645	2,063	1,582
Interest expense	(1,249)	(951)	(298)
Foreign exchange (loss) gain	(4,963)	(6,442)	1,479
Loss before income taxes	(291,370)	(171,491)	(119,879)
Income tax (benefit) expense	3,797	(1,032)	4,829
Net loss	$ (295,167)	$ (170,459)	$ (124,708)

Product net sales

Our product net sales include sales of Epidiolex, which we launched in the United States in November 2018 and began to sell in certain European markets in late 2019, and sales of Sativex outside of the United States pursuant to license agreements with commercial partners. We also sell Epidiolex through certain early access programs outside of the United States.

Product net sales for the year ended December 31, 2019 were comprised of $296.4 million in net sales of Epidiolex and $13.9 million in net sales of Sativex. The $295.4 million increase in product net sales to $310.3 million for the year ended December 31, 2019 compared to $14.9 million for the year ended December 31, 2018 was primarily due to the November 2018 launch of Epidiolex in the United States.

Product net sales in the three months ended December 31, 2018 were comprised of $4.7 million in net sales of Epidiolex and $1.9 million in net sales of Sativex. The $4.4 million increase in product net sales to $6.6 million for the three months ended December 31, 2018 compared to $2.2 million for the three months ended December 31, 2017 was primarily due to the November 2018 launch of Epidiolex in the United States.

Product net sales increased $2.5 million in the year ended September 30, 2018 to $10.5 million compared to $8.0 million in the year ended September 30, 2017. The increase in product net sales in the year ended September 30, 2018 was primarily due to increases in sales of Sativex in Europe, Canada and Israel.

Other revenue

Other revenue primarily consists of milestone revenue related to our Sativex license agreements and research and development fee revenue related to license and collaboration agreements.

Other revenue in the year ended December 31, 2019 and 2018 consists of remaining development fees related to the Otsuka license agreement.

Other revenue in the three months ended December 31, 2018 consists of remaining development fees related to the Otsuka license agreement. Other revenue in the three months ended December 31, 2017 primarily consists of previously deferred development fee revenue that was recognized upon the termination of the Otsuka license agreement. The reduction in other revenue in the three months ended December 31, 2018 compared to the three months ended December 31, 2017 was primarily due to the termination of the Otsuka license agreement which occurred in December of 2017.

Other revenue in the year ended September 30, 2018 consists of $2.1 million of research and development fee revenue related to the Otsuka license agreement that was terminated in the first quarter of the fiscal year ended September 30, 2018 and $0.2 million of milestone revenue related to the achievement of a Sativex regulatory approval milestone. Other revenue in the year ended September 30, 2017 consists of $0.7 million of research and development fees related to the Otsuka license agreement. The increase in development fee revenue in the year ended September 30, 2018 is due to deferred research and development fees that were recognized in the fiscal year ended September 30, 2018 in conjunction with the termination of the Otsuka license agreement.

Cost of product sales

Cost of sales increased $20.6 million, or 309%, in the year ended December 31, 2019 to $27.2 million, or 9% of product net sales, compared to $6.6 million, or 45% of product net sales in the year ended December 31, 2018. The increase in cost of sales in dollars is primarily due to an increase in product net sales, primarily due to the launch of Epidiolex in the U.S. The reduction in cost of sales as a percentage of product net sales is due to the positive impact of directly commercializing Epidiolex in the U.S. in the year ended December 31, 2019. In the year ended December 31, 2018, the majority of product net sales were sales of Sativex outside of the U.S. through license partners.

Cost of sales increased $0.7 million, or 56% in the three months ended December 31, 2018 to $1.8 million, or 28% of product net sales, compared to $1.2 million, or 53% of product net sales in the three months ended December 31, 2017. The increase in cost of sales in dollars is primarily due to an increase in product net sales, which is primarily due to the launch of Epidiolex in the U.S. The reduction in cost of sales as a percentage of product net sales is due to the positive impact in the three months ended December 31, 2018 of directly commercializing Epidiolex in the U.S. compared to the similar period in the prior year when products net sales consisted only of Sativex sales outside of the U.S. through license partners.

Cost of sales increased $1.5 million, or 32%, in the year ended September 30, 2018 to $6.0 million, or 57% of product net sales, compared to $4.5 million, or 57% of product net sales in the year ended September 30, 2017. The increase in cost of sales in dollars is primarily due to the increase in product net sales in the year ended September 30, 2018 compared to the year ended September 30, 2017.

Research and development expenses

We believe that our future revenues and cash flows are most likely to be affected by the successful development and approval of our significant late-stage research and development candidates. As of December 31, 2019, we consider the following research and development projects to be our most significant late-stage product candidates:

- Epidiolex for the treatment of tuberous sclerosis complex (United States and Europe)
- Nabiximols for spasticity associated with MS (United States)

On September 23, 2019, we announced that the European Commission approved the marketing authorization for Epidyolex in Europe. We have received Orphan Designation from the European Commission for Orphan Medicinal Products for Epidyolex for Dravet syndrome and LGS.

We have completed our Phase 3 trial of Epidiolex for the treatment of TSC. In May 2019, we reported positive top-line Phase 3 results and in December 2019 we reported additional positive trial data. On February 3, 2020, we announced that we submitted a supplemental new drug application with the FDA for this indication, and we, expect to seek supplemental approval in Europe in early 2020.

In December 2017, we terminated our license agreement with Otsuka and we have reacquired full ownership of the development and commercialization rights to nabiximols in the United States. We have had several meetings with the FDA to discuss the optimal regulatory pathway for U.S. approval of nabiximols and are now in the process of planning an additional clinical program, which is expected to commence in early 2020.

Research and development expenses consist of internal and external costs to conduct our pre-clinical studies and clinical trials, payroll costs associated with employing our team of research and development staff, share-based payment expenses, property costs associated with leasing laboratory and office space to accommodate our research teams, costs of growing botanical raw material, costs of processing product for clinical trials, costs of consumables used in the conduct of our in-house research programs, payments for research work conducted by sub-contractors and sponsorship of work by our network of academic collaborative research scientists, costs associated with safety studies and costs associated with the development of Epidiolex, Sativex, and our other pipeline product candidates. Research and development expense is presented net of reimbursements from reimbursable tax and expenditure credits from the U.K. government.

We track all research and development expenditures against detailed budgets but do not seek to allocate all research and development costs by individual project. In 2018, we began to track external third-party costs for clinical trials by product candidate. In prior years we tracked costs for historical nabiximols projects funded by Otsuka, but other costs were not allocated to individual projects. The components of R&D expense for the years ended December 31, 2019 and 2018, three months ended December 31, 2018 and 2017 and the year ended September 30, 2018 are as follows:

	Years Ended December 31,		Three Months Ended December 31,		Year Ended September 30,
	2019	2018	2018	2017	2018
			(in thousands)		
External clinical trial expense					
Epidiolex	$ 28,020	$ 33,970	$ 8,936	$ 7,508	$ 33,262
Nabiximols	$ 3,837	$ 33	$ 69	$ 45	—
Other programs	8,413	2,645	770	296	1,460
Total external clinical trial expense	40,270	36,648	9,775	7,849	34,722
Otsuka funded research and development	—	565	—	—	565
Research and development tax and expense credits	(3,992)	(4,090)	(759)	(994)	(4,325)
Other internal research and development	106,400	113,504	20,070	29,340	122,774
Total research and development expense	$ 142,678	146,627	$ 29,086	$ 36,195	$ 153,736

The components of R&D expense for the years ended September 30, 2017, are as follows:

	Year Ended September 30, 2017
	(in thousands)
Otsuka funded research and development	$ 669
Other research and development	137,587
Research and development tax and expense credits	(26,007)
Total research and development expense	$ 112,249

R&D expenses decreased $3.9 million, or 3%, to $142.7 million for the year ended December 31, 2019 compared to $146.6 million the year ended December 31, 2018. R&D expenses decreased $7.1 million, or 20%, to $29.1 million for the three months ended December 31, 2018 compared to $36.2 million the three months ended December 31, 2017. The decrease in R&D expenses in both periods was primarily due to the prior period impact of inventory production costs for Epidiolex that were charged to R&D expenses prior to FDA approval in June 2018.

R&D expenses increased $41.5 million, or 37.0%, to $153.7 million in the year ended September 30, 2018 compared to $112.2 million in the year ended September 30, 2017. The increase in R&D expenses was primarily due to an increase in personnel and related costs, including share-based compensation expense, related to an increase in our global R&D headcount, an increase in costs to prepare the Epidiolex regulatory submissions in the U.S. and Europe, an increase in costs of growing high CBD plant material for Epidiolex, which prior to the achievement of regulatory approval in the U.S. were included in R&D expenses, and a decrease in the U.K. research and development tax and expense credits due to the transition out of the SME scheme and into the RDEC scheme in the U.K.

Sales, general and administrative expenses

Sales, general and administrative, or SG&A, expenses consist primarily of salaries and benefits related to our executive, commercial, and corporate support functions, expenses associated with our commercial activities, and other general administration expenses. We expect that sales, general and administrative expenses will increase in the future as we expand our operating activities and continue to build our commercial team in preparation for the launch of Epidiolex in additional markets in Europe.

SG&A expenses increased $94.2 million, or 57%, to $259.9 million in the year ended December 31, 2019 compared to $165.7 million in 2018. The increase in SG&A expenses in 2019 was primarily due to an increase in employee-related expenses driven by the build-out of our commercial functions in the United States and Europe, costs related to the launch of Epidiolex in Europe, an increase in our corporate support functions, and an increase in insurance expenses.

SG&A expenses increased $23.9 million, or 95%, to $49.1 million in three months ended December 31, 2018 compared to $25.2 million in 2017. The increase in SG&A expenses in 2018 was primarily due to an increase in employee-related expenses driven by the build-out of our commercial functions in the U.S. and Europe, costs related to the November 2018 launch of Epidiolex in the U.S., an increase in all of our corporate support functions, and, to a smaller degree, an increase in insurance expenses and an increase audit and legal fees related to our transition to domestic registrant status with the SEC.

SG&A expenses increased $83.8 million, or 144.4%, to $141.8 million in the year ended September 30, 2018 compared to $58.0 million in the year ended September 30, 2017. The increase in SG&A expenses in 2018 was primarily due to an increase in employee-related expenses driven by the build-out of our commercial functions in the U.S. and Europe, pre-launch costs related to the November 2018 launch of Epidiolex in the U.S., an increase in all of our corporate support functions, and, to a smaller degree, an increase in insurance expenses and an increase audit and legal fees related to our transition to domestic registrant status with the SEC.

Interest Income

Interest income increased $3.0 million in the year ended December 31, 2019 to $8.5 million compared to interest income of $5.5 million in the year ended December 31, 2018. The increase in interest income in 2019 is primarily due to higher average cash and cash equivalent balances in 2019 compared to 2018 and an increase in interest rates on money market funds during the period.

Interest income increased $1.8 million in the three months ended December 31, 2018 to $2.4 million compared to interest income of $0.6 million during the three months ended December 31, 2017. The increase in interest income in 2018 is primarily due to higher average cash and cash equivalent balances in 2018 compared to 2017 and increases in interest rates on money market funds during the period.

Interest income increased $1.5 million in the year ended September 30, 2018 to $3.6 million compared to interest income of $2.1 million in the year ended September 30, 2017. The increase in interest income in 2018 is primarily due to higher average cash and cash equivalent balances in 2018 compared to 2017 and a small increase in interest rates during the period.

Interest Expense

Interest expense for the year ended December 31, 2019 was $1.1 million and interest expense for the year ended December 31, 2018 was $1.2 million. Interest expense is primarily related to our finance lease liabilities, which did not significantly fluctuate in 2019 compared to 2018.

Interest expense remained consistent during the three months ended December 31, 2018 of $0.3 million compared to interest expense of $0.3 million in the three months ended December 31, 2017.

Interest expense increased $0.2 million in the year ended September 30, 2018 to $1.2 million compared to interest expense of $1.0 million in the year ended September 30, 2017. The increase in interest expense in 2018 is primarily due to the increase in finance lease liabilities in 2018 compared to 2017.

Other income

Other income for the year ended December 31, 2019 consisted of $104.1 million in net proceeds from the sale of the priority review voucher that we received from the FDA in connection with the approval of Epidiolex in the United States.

Foreign currency exchange loss

Foreign currency exchange gains and losses are driven primarily by financial assets and liabilities denominated in a currency other than the transacting entity's functional currency. A significant majority of our cash balances are denominated in U.S. dollars and the functional currency of the GW Pharmaceuticals plc legal entity for the year ended September 30, 2017 was the British Pound. Accordingly, a substantial portion of foreign currency transaction losses in the year ended September 30, 2017 were related to the impact of exchange rate changes between the U.S. dollar and British Pound on the U.S. dollar denominated cash deposits held by GW Pharmaceuticals plc. On October 1, 2017, the U.S. dollar became the functional currency of GW Pharmaceuticals plc. Beginning on October 1, 2017, our primary exposure to foreign currency exchange gains and losses is the British Pound denominated cash balances held by GW Pharmaceuticals plc and intercompany balances between subsidiaries with different functional currencies.

Foreign currency exchange loss for the year ended December 31, 2019 was $2.3 million compared to a foreign currency exchange loss of $6.1 million in the year ended December 31, 2018. The decrease in the foreign exchange loss in 2019 was due primarily to a smaller year over year change in the foreign currency exchange rates of the U.S. dollar and British Pound compared to the change in rates for the similar period in 2018.

Foreign currency exchange loss for the three months ended December 31, 2018 was $1.0 million compared to a foreign currency exchange gain of $0.2 million in the three months ended December 31, 2017. The increase in the foreign exchange loss in the three months ended December 31, 2018 compared to the prior year period was due primarily to a due to a strengthening of the U.S. dollar against the British Pound in the three months ended December 31, 2018.

Foreign currency exchange loss for the year ended September 30, 2018 was $5.0 million compared to a foreign currency exchange loss of $6.4 million in the year ended September 30, 2017. The decrease in the foreign exchange loss in 2018 was due primarily to a change in our foreign currency exchange rate exposure due to the U.S. dollar becoming the functional currency of GW Pharmaceuticals plc on October 1, 2017.

Income tax expense (benefit)

Income tax benefit for both the year ended December 31, 2019 and the year ended December 31, 2018 was $0.2 million. An increase in the income tax benefit in December 31, 2019 primarily related to excess tax benefits for stock compensation was fully offset by an increase in state taxes.

Income tax benefit for the three months ended December 31, 2018 was $0.3 million compared to an income tax expense of $3.7 million for the three months ended December 31, 2017. The decrease in income tax expense for 2018 was primarily due to the remeasurement of the federal portion of our U.S. subsidiary's deferred tax assets and liabilities recorded in the three months ended December 31, 2017, the period of enactment of the Tax Cuts and Jobs Act.

Income tax expense for the year ended September 30, 2018 was $3.8 million compared to an income tax benefit of $1.0 million for the year ended September 30, 2017. The increase in income tax expense for 2018 was primarily due to the remeasurement of the federal portion of our U.S. subsidiary's deferred tax assets and liabilities to the enacted tax rate expected to apply when the temporary differences are to be realized. The President of the United States signed into law the Tax Cuts and Jobs Act on December 22, 2017 which among a broad range of tax reform measures, reduced the corporate tax rate from 35% to 21% effective January 1, 2018. The negative impact of the remeasurement of deferred tax assets was partially offset by a reduction in taxes on current period income due to the decline in the U.S. statutory tax rate.

Liquidity and Capital Resources

In recent years, we have incurred significant net losses and negative cash flows from operations. We have largely funded our operations from issuances of equity securities, government expense and tax credits, and the sale of our priority review voucher. Our cash flows may fluctuate, are difficult to forecast and will depend on many factors, including:

- the timing of achievement of future Epidiolex regulatory approvals and commercial launches in the United States and Europe;
- the extent to which we seek to retain development rights to our pipeline of new product candidates or whether we seek to out-license them to a partner who will fund future research and development expenditure in return for a right to share in future commercial revenue;
- the extent of success in our early pre-clinical and clinical stage research programs which will determine the amount of funding required to further the development of our product candidates;
- the terms and timing of new strategic collaborations;
- the number and characteristics of the product candidates that we seek to develop;
- the outcome, timing and cost of regulatory approvals of our product candidates;
- the costs involved in filing and prosecuting patent applications and enforcing and defending potential patent claims; and
- the costs of hiring additional skilled employees to support our continued growth.

We believe that our cash and cash equivalents as of December 31, 2019 of $536.9 million will be sufficient to fund our operations, including currently anticipated research and development activities and planned capital expenditures, for the foreseeable future, including for at least the next 12 months.

Cash Flows

The following table summarizes the results of our cash flows for the years ended December 31, 2019 and 2018, three months ended December 31, 2018 and 2017 and years ended September 30, 2018 and 2017.

	Years Ended December 31,		Three Months Ended December 31,		Years Ended September 30,	
	2019	2018	2018	2017	2018	2017
	(in thousands)					
Net cash used in operating activities	$ (123,469)	$ (254,770)	$ (74,460)	$ (51,558)	$ (231,868)	$ (148,974)
Net cash provided by (used in) investing activities	61,629	$ (42,896)	(18,750)	(8,741)	(32,887)	(20,097)
Net cash provided by (used in) financing activities	1,946	$ 324,479	324,468	297,743	297,754	(1,213)
Cash and cash equivalents at end of the year	$ 536,933	$ 591,497	$ 591,497	$ 559,227	$ 354,913	$ 322,154

Operating activities

As of December 31, 2019, we had cash and cash equivalents totaling $536.9 million compared to $591.5 million as of December 31, 2018. Net cash used in operating activities decreased by $131.3 million to $123.5 million during the year ended December 31, 2019 compared to $254.8 million for the year ended December 31, 2018. The decrease in cash used is attributable to a $295.4 million increase in net product sales, partially offset by a $20.6 million increase in cost of product sales, a $94.2 million increase in SG&A expenses, and a $60.1 million increase in cash used to fund changes in net operating assets and liabilities.

Net cash used in operating activities increased by $22.9 million to $74.5 million during the three months ended December 31, 2018 compared to $51.6 million for the three months ended December 31, 2017. The increase in cash used is primarily attributable to net loss of $72.2 million adjusted for non-cash items, including depreciation and amortization expense of $2.5 million and stock-based compensation of $9.7 million.

Net cash used in operating activities increased by $82.9 million to $231.9 million for the year ended September 30, 2018 compared to $149.0 million for the year ended September 30, 2017. The increase in cash used in operating activities was primarily due to the increase in research and development expenses, including the cost of growing high CBD plant material for Epidiolex prior to the achievement of regulatory approval in the U.S., and increased SG&A expenses related to the ramp up of commercialization activities and corporate support functions.

Investing activities

Net cash provided by investing activities increased by $104.5 million to $61.6 million during the year ended December 31, 2019 compared to net cash used in investing activities of $42.9 million for the year ended December 31, 2018. The increase in cash provided by investing activities is primarily due to the sale of our priority review voucher in April 2019.

Net cash used in investing activities increased by $10.1 million to $18.8 million during the three months ended December 31, 2018 compared to $8.7 million for the three months ended December 31, 2017. The increase in cash used in investing activities is primarily due to the continued expansion of our manufacturing facilities.

Net cash used in investing activities increased by $12.8 million to $32.9 million for the year ended September 30, 2018 compared to $20.1 million for the year ended September 30, 2017. The increase in cash used in investing activities was primarily due to the continued expansion of our manufacturing facilities.

Financing activities

Financing activities provided a decrease in net cash of $322.5 million to $1.9 million during the year ended December 31, 2019 compared to $324.5 million during the year ended December 31, 2018. The decrease in cash provided by financing activities is primarily due to the net proceeds of $324.6 million received from our equity offering in October 2018.

Financing activities provided an increase in net cash of $26.8 million to $324.5 million during the three months ended December 31, 2018 compared to $297.7 million during the three months ended December 31, 2017. The increase in cash provided by financing activities is primarily due to net proceeds of $324.6 million received from our equity offering in October 2018.

Net cash provided by financing activities increased by $298.9 million to $297.7 million for the year ended September 30, 2018 compared to cash used in financing activities of $1.2 million for the year ended September 30, 2017. The increase in cash provided by financing activities was primarily due to net proceeds of $297.9 million from our equity offering in December 2017.

Equity Financings

In October 2018, we completed a public offering of ADSs in which we sold 26.2 million ordinary shares at an offering price of $158.00 per ADS. The ADSs were sold pursuant to a shelf registration statement with the SEC. The net proceeds generated from this transaction, after underwriting discounts and commissions and offering costs, were approximately $324.6 million.

In December 2017, we completed a public offering of ADSs in which we sold 33.1 million ordinary shares at an offering price of $115.00 per ADS. The ADSs were sold pursuant to a shelf registration statement with the SEC. The net proceeds generated from this transaction, after underwriting discounts and commissions and offering costs, were approximately $297.9 million.

Off Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Tabular Disclosure of Contractual Obligations

The following table summarizes our contractual obligations as at December 31, 2019.

	Payments Due by Period				
	Total	Less than 1 year	1 – 3 years	3 – 5 years	More than 5 years
	(in thousands)				
Operating lease obligations	$ 34,917	$ 5,900	$ 10,097	$ 7,483	$ 11,437
Finance lease obligations	9,788	729	1,450	1,436	6,173
Purchase obligations	38,975	23,126	13,874	658	1,317
Landlord financing obligations	14,143	1,266	2,532	2,532	7,813
Total contractual obligations	$ 97,823	$ 31,021	$ 27,953	$ 12,109	$ 26,740

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risks in the ordinary course of our business, which are principally limited to foreign currency exchange rate fluctuations, particularly between the British Pound and the U.S. dollar, and credit risk. These risks are managed by maintaining an appropriate mix of cash deposits and securities in various currencies, placed with a variety of financial institutions for varying periods according to expected liquidity requirements.

Interest Rate Risk

We are exposed to interest rate risk on cash and cash equivalents. The primary objective of our investment activities is to preserve principal while at the same time maximizing yields without significantly increasing risk. To achieve this objective, we invest in highly liquid and high-quality government and other debt securities. To minimize our exposure due to adverse shifts in interest rates, we invest in short-term securities. Due to the short holding period of our investments and the nature of our investments, we have concluded that we do not have a material financial market risk exposure.

Currency Risk

We are exposed to currency exchange rate risk because we currently operate in the United Kingdom and the United States. Our manufacturing operations and a substantial portion of our research and development costs are incurred in our U.K.-based subsidiaries and are generally denominated in British Pounds, which is also the functional currency of the U.K.-based subsidiaries. The functional currency of GW Pharmaceuticals plc and our U.S. subsidiary is the U.S. dollar. We do not use forward exchange contracts to manage currency exchange rate exposure.

Item 8. Financial Statements and Supplementary Data.

The consolidated financial statements required pursuant to this item are included in Item 15 of this report and are presented beginning on page F-1.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Disclosure Controls and Procedures.

As required by Rule 13a-15 under the Exchange Act, management, including our Chief Executive Officer and our Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this report. Disclosure controls and procedures refer to controls and other procedures designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in our reports that we file or submit under the Exchange Act is accumulated and communicated to management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding our required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on the foregoing, our Chief Executive Officer and our Chief Financial Officer have concluded that, as of December 31, 2019, our disclosure controls and procedures in internal control over financial reporting were effective.

Management's Annual Report on Internal Control over Financial Reporting.

Management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) under the Exchange Act. Our internal control over financial reporting is a process to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. GAAP. We have a program for the review of our internal control over financial reporting to ensure compliance with the requirements of the Exchange Act and Section 404 of the Sarbanes-Oxley Act. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. GAAP, as issued by FASB;
- provide reasonable assurance that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect all misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2019. In conducting its assessment of internal control over financial reporting, management based its evaluation on the *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission as at December 31, 2019. Based on its evaluation, our management has concluded that our internal control over financial reporting was effective as of December 31, 2019.

Attestation Report of the Registered Public Accounting Firm

Our internal control over financial reporting as of December 31, 2019 has been audited by Deloitte & Touche LLP. Their audit report on internal control over financial reporting appears in Part IV, Item 15. Deloitte & Touche LLP has also audited the consolidated financial statements as of and for the year ended December 31, 2019 and their report expressed an unqualified opinion on those financial statements.

Changes in Internal Control Over Financial Reporting

There have been no changes in our internal control over financial reporting identified in connection with the evaluation described above in "Internal Control Over Financial Reporting" that occurred during the quarter ended December 31, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, to be filed with the Commission not later than 120 days after the close of our fiscal year ended December 31, 2019.

Item 11. Executive Compensation

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, to be filed with the Commission not later than 120 days after the close of our fiscal year ended December 31, 2019

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, to be filed with the Commission not later than 120 days after the close of our fiscal year ended December 31, 2019.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, to be filed with the Commission not later than 120 days after the close of our fiscal year ended December 31, 2019.

Item 14. Principal Accounting Fees and Services

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, to be filed with the Commission not later than 120 days after the close of our fiscal year ended December 31, 2019.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) 1. Financial Statements

As part of this Annual Report on Form 10-K, the consolidated financial statements are listed in the accompanying index to financial statements on page F-1.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable, or the required information is shown in the Financial Statements or notes thereto.

3. Exhibit Index

The following is a list of exhibits filed as part of this Annual Report on Form 10-K or are incorporated herein by reference:

Exhibit Number	Description of Exhibit
3.1 *	Amended and Restated Memorandum & Articles of Association of GW Pharmaceuticals plc (incorporated by reference to Exhibit 3.1 to our Annual Report on Form 10-K filed with the SEC on November 29, 2018).
4.1 *	Form of specimen certificate evidencing ordinary shares (incorporated by reference to Exhibit 4.1 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
4.2(1)*	Form of Deposit Agreement among GW Pharmaceuticals plc, Citibank, N.A., as the depositary bank and all Holders and Beneficial Owners of ADSs issued thereunder (incorporated by reference to Exhibit 4.2 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
4.3(1)*	Form of American Depositary Receipt (included in Exhibit 2.2) (incorporated by reference to Exhibit 4.3 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
4.4 **	Description of Securities Registered under Section 12 of the Securities Exchange Act of 1934.
10.1 †*	Research Collaboration and Licence Agreement between GW Pharma Limited. and GW Pharmaceuticals plc and Otsuka Pharmaceutical Co., Ltd., dated July 9, 2007 (incorporated by reference to Exhibit 10.16 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.2 †*	Amendment No. 1 to Research Collaboration and Licence Agreement, dated March 14, 2008 (incorporated by reference to Exhibit 10.17 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.3 †*	Amendment No. 2 to Research Collaboration and Licence Agreement, dated June 29, 2010 (incorporated by reference to Exhibit 10.18 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.4 †*	Development and Licence Agreement between GW Pharma Limited. and GW Pharmaceuticals Plc and Otsuka Pharmaceutical Co., Ltd., dated February 14, 2007 (incorporated by reference to Exhibit 10.19 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.5 †*	Amendment No. 1 to Development and Licence Agreement, dated November 1, 2008 (incorporated by reference to Exhibit 10.20 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.6 †*	Letter amending Development and Licence Agreement, dated October 21, 2010 (incorporated by reference to Exhibit 10.21 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.7 †*	Production Supply Agreement, dated March 7, 2007 (incorporated by reference to Exhibit 10.24 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.8 †*	Lease, dated July 6, 2009 (incorporated by reference to Exhibit 10.25 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).

Exhibit Number	Description of Exhibit
10.9 †*	Lease, dated October 9, 2009 (incorporated by reference to Exhibit 10.26 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.10 †*	Lease, dated April 6, 2011 (incorporated by reference to Exhibit 10.27 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.11 †*	Lease, dated October 12, 2011 (incorporated by reference to Exhibit 10.28 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.12 †*	Lease, dated January 6, 2012 (incorporated by reference to Exhibit 10.29 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.13 †*	Agreement for Lease, dated April 4, 2012 (incorporated by reference to Exhibit 10.30 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.14 *	Occupational Underlease, dated August 11, 2010 (incorporated by reference to Exhibit 10.31 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.15 *	Lease, dated May 24, 2011 (incorporated by reference to Exhibit 10.32 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.16 *	Tenancy Agreement, dated November 19, 2012 (incorporated by reference to Exhibit 10.33 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.17 *	Service Agreement by and between GW Research Limited and Dr. Geoffrey Guy, dated March 14, 2013 (incorporated by reference to Exhibit 10.36 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.18 *	Service Agreement by and between GW Research Limited and Justin Gover, dated February 26, 2013 (incorporated by reference to Exhibit 10.37 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.19 *	Letter of Appointment by and between GW Pharmaceuticals plc and James Noble, dated February 26, 2013 (incorporated by reference to Exhibit 10.39 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.20 *	Letter of Appointment by and between GW Pharmaceuticals plc and Thomas Lynch, dated February 26, 2013 (incorporated by reference to Exhibit 10.40 to our Registration Statement on Form F-1 (file no. 333-187356), as amended, initially filed with the SEC on March 19, 2013).
10.21 *	Service Agreement by and between Greenwich Biosciences, Inc. (formerly GW Pharmaceuticals Inc.) and Cabot Brown, dated November 7, 2013 (incorporated by reference to Exhibit 4.41 to our Annual Report on Form 20-F (file no. 001-35892), filed with the SEC on November 25, 2013).
10.22 *	Long Term Incentive Plan (incorporated by reference to Exhibit 4.1 to our Registration Statement on Form S-8 (file no. 333-204389), filed with the SEC on May 22, 2015).
10.23 †*	Lease, dated May 24, 2013 (incorporated by reference to Exhibit 4.46 to our Annual Report on Form 20-F (file no. 001-35892), as amended, originally filed with the SEC on November 25, 2013).
10.24 †*	Lease, dated May 24, 2013 (incorporated by reference to Exhibit 4.47 to our Annual Report on Form 20-F (file no. 001-35892), as amended, originally filed with the SEC on November 25, 2013).
10.25 †*	Lease, dated May 24, 2013 (incorporated by reference to Exhibit 4.48 to our Annual Report on Form 20-F (file no. 001-35892), as amended, originally filed with the SEC on November 25, 2013).
10.26 *	Lease, dated August 1, 2013 (incorporated by reference to Exhibit 4.49 to our Annual Report on Form 20-F (file no. 001-35892), as amended, originally filed with the SEC on November 25, 2013).
10.27 *	Lease, dated July 16, 2013 (incorporated by reference to Exhibit 4.50 to our Annual Report on Form 20-F (file no. 001-35892), as amended, originally filed with the SEC on November 25, 2013).
10.28 *	Transfer of Contract, dated July 20, 2015 among GW Pharmaceuticals plc, GW Research Limited and Justin Gover (incorporated by reference to Exhibit 4.53 to our Annual Report on Form 20-F (file no. 001-35892) filed with the SEC on December 7, 2015).

Exhibit Number	Description of Exhibit
10.29 *	Offer Letter, dated July 17, 2015 between Greenwich Biosciences, Inc. (formerly GW Pharmaceuticals Inc.) and Justin Gover (incorporated by reference to Exhibit 4.54 to our Annual Report Form 20-F (file no. 001-35892) filed with the SEC on December 7, 2015).
10.30 †*	Lease, dated May 27, 2016 (incorporated by reference to Exhibit 4.58 to our Annual Report Form 20-F (file no. 001-35892) filed with the SEC on December 5, 2016).
10.31 †*	Amended and Restated Production and Supply Agreement, dated August 31, 2016, among GW Pharma Limited, GW Pharmaceuticals plc and British Sugar plc (incorporated by reference to Exhibit 4.59 to our Annual Report (file no. 001-35892) filed with the SEC on December 5, 2016).
10.32 *	Letter of Appointment by and between GW Pharmaceuticals plc and Cabot Brown, effective January 1, 2016 (incorporated by reference to Exhibit 4.61 to our Annual Report (file no. 001-35892) filed with the SEC on December 5, 2016).
10.33 *	Letter of Appointment by and between GW Pharmaceuticals plc and James Noble, effective February 1, 2016 (incorporated by reference to Exhibit 4.62 to our Annual Report (file no. 001-35892) filed with the SEC on December 5, 2016).
10.34 *	Fee Letter, dated April 10, 2017 from GW Pharmaceuticals plc to Cabot Brown (incorporated by reference to Exhibit 4.63 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.35 *	Fee Letter, dated April 10, 2017 from GW Pharmaceuticals plc to James Noble (incorporated by reference to Exhibit 4.64 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.36 *	Salary and Bonus Letter, dated April 13, 2017 from GW Pharmaceuticals plc to Geoffrey Guy (incorporated by reference to Exhibit 4.66 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.37 *	Greenwich Biosciences, Inc. Compensation Memo, dated February 21, 2017 to Justin Gover (incorporated by reference to Exhibit 4.69 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.38 *	Offer Letter, dated February 20, 2017 between Greenwich Biosciences, Inc. and Scott Giacobello (incorporated by reference to Exhibit 4.71 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.39 *	Offer Letter, dated April 20, 2017 between Greenwich Biosciences, Inc. and Volker Knappertz (incorporated by reference to Exhibit 4.72 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.40 *	Offer Letter, dated May 5, 2017 between Greenwich Biosciences, Inc. and Douglas Snyder(incorporated by reference to Exhibit 4.73 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.41 *	Relocation Assistance Agreement, dated May 8, 2017 between Greenwich Biosciences, Inc. and Douglas Snyder (incorporated by reference to Exhibit 4.74 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.42 *	Greenwich Biosciences, Inc. Change in Control and Severance Benefit Plan (incorporated by reference to Exhibit 4.75 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.43 *	Change in Control and Severance Benefit Plan Participation Agreement, dated July 13, 2017 between Greenwich Biosciences, Inc. and Volker Knappertz (incorporated by reference to Exhibit 4.77 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.44 *	Change in Control and Severance Benefit Plan Participation Agreement, dated August 2, 2017 between Greenwich Biosciences, Inc. and Scott Giacobello (incorporated by reference to Exhibit 4.78 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.45 *	Change in Control and Severance Benefit Plan Participation Agreement, dated August 9, 2017 between Greenwich Biosciences, Inc. and Douglas Snyder (incorporated by reference to Exhibit 4.79 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.46 *	Master Services Agreement, dated April 1, 2017 between GW Research Ltd and inVentiv Health Commercial Europe Limited (incorporated by reference to Exhibit 4.80 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.47 †*	Master Statement of Work, dated June 15, 2017 between GW Research Ltd and inVentiv Health Commercial Europe Limited (incorporated by reference to Exhibit 4.81 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).

Exhibit Number	Description of Exhibit
10.48 †*	Contract for the Design, Construction, Testing and Commissioning of GW Pharma Building 750B and Process Equipment at Kent Science Park, dated September 7, 2017 between GW Pharma Limited and The Austin Company of (U.K.) Limited (incorporated by reference to Exhibit 4.83 to our Annual Report on Form 20-F, filed with the SEC on December 4, 2017).
10.49 *	Letter of Appointment by and between GW Pharmaceuticals plc and Catherine Mackey, dated December 20, 2017 (incorporated by reference to Exhibit 10.80 to our Annual Report on Form 10-K filed with the SEC on November 29, 2018).
10.50 *	Letter of Appointment by and between GW Pharmaceuticals plc and Alicia Secor, dated December 20, 2017 (incorporated by reference to Exhibit 10.81 to our Annual Report on Form 10-K filed with the SEC on November 29, 2018).
10.51 *	Letter of Appointment by and between GW Pharmaceuticals plc and Lord William Waldegrave, dated December 20, 2017 (incorporated by reference to Exhibit 10.82 to our Annual Report on Form 10-K filed with the SEC on November 29, 2018).
10.52 *	Long Term Incentive Plan (incorporated by reference to Exhibit 4.1 to our Registration Statement on Form S-8 (file no. 333-217328), filed with the SEC on April 17, 2017).
10.53 *	Offer letter by and between Greenwich Biosciences, Inc. and Darren Cline (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed with the SEC on April 12, 2019).
14.1*	Code of Ethics (incorporated by reference to Exhibit 14.1 to our Annual Report on Form 10-K filed with the SEC on November 29, 2018).
16.1*	Letter of Deloitte LLP, dated November 28, 2018 (incorporated by reference to Exhibit 16.1 to our Annual Report on Form 10-K filed with the SEC on November 29, 2018).
21.1**	List of Subsidiaries
23.1**	Consent of Deloitte LLP
23.2**	Consent of Deloitte & Touche LLP
31.1**	Certificate of Chief Executive Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to §302 of the Sarbanes-Oxley Act of 2002.
31.2**	Certificate of Chief Financial Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to §302 of the Sarbanes-Oxley Act of 2002.
32.1***	Certificate of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002.
101***	INS Inline XBRL Instance Document
101***	SCH Inline XBRL Taxonomy Extension Schema Document
101***	CAL Inline XBRL Taxonomy Calculation Linkbase Document
101***	DEF Inline XBRL Taxonomy Extension Definition Linkbase Document
101***	LAB Inline XBRL Taxonomy Label Linkbase Document
101***	PRE Inline XBRL Taxonomy Presentation Linkbase Document
104***	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101).

* Previously filed.
** Filed herewith.
*** Furnished herewith.
† Confidential treatment previously requested and granted as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.
(1) Incorporated by reference to the Registration Statement on Form F-6 (File No. 333-187978), filed with the Securities and Exchange Commission on April 18, 2013 with respect to ADSs representing Ordinary Shares.

Item 16. Form 10-K Summary

None.

Signature

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

GW PHARMACEUTICALS PLC

By: /s/Justin Gover

Name: Justin Gover

Title: *Chief Executive Officer*

Date: February 27, 2020

POWER OF ATTORNEY AND SIGNATURES

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Dr. Geoffrey Guy, Justin Gover and Scott Giacobello, and each of them, as his and her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Justin Gover Justin Gover	Chief Executive Officer and Director (Principal Executive Officer)	February 27, 2020
/s/ Scott Giacobello Scott Giacobello	Chief Financial Officer (Principal Financial and Accounting Officer)	February 27, 2020
/s/ Geoffrey Guy Dr. Geoffrey Guy	Director	February 27, 2020
/s/ James Noble James Noble	Director	February 27, 2020
/s/ Cabot Brown Cabot Brown	Director	February 27, 2020
/s/ Thomas Lynch Thomas Lynch	Director	February 27, 2020
/s/ Catherine Mackey Dr. Catherine Mackey	Director	February 27, 2020
/s/ Alicia Secor Alicia Secor	Director	February 27, 2020
/s/ William Waldegrave Lord William Waldegrave	Director	February 27, 2020

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of GW Pharmaceuticals plc

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of GW Pharmaceuticals plc and subsidiaries (the "Company") as of December 31, 2019 and 2018, the related consolidated statements of operations, comprehensive income (loss), stockholders' equity, and cash flows, for the year ended December 31, 2019, three month period ended December 31, 2018, and year ended September 30, 2018, and the related notes (collectively referred to as the "financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for the year ended December 31, 2019, three month period ended December 31, 2018, and year ended September 30, 2018, in conformity with accounting principles generally accepted in the United States of America. Also, in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by COSO.

Basis for Opinions

The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on these financial statements and an opinion on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the financial statements included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures to respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current-period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Epidiolex Product Net Sales — Rebates — Refer to Note 2 to the financial statements

Critical Audit Matter Description

As more fully disclosed in Note 2 to the financial statements, the Company recognizes revenue from product sales, net of allowances for rebates, which are included in accrued liabilities on the consolidated balance sheet. Allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program and the Medicare Part D prescription drug benefit as well as contractual rebates with commercial payers. The allowance for rebates is based on contracted or statutory discount rates and expected utilization by benefit plan participants.

Given the significant estimation and uncertainty involved in management's assumptions to calculate the rebates, such as consideration of historical claims experience, expected utilization, unbilled claims, and claims submission time lags, and the limited historical data currently available, auditing these estimates involved especially subjective judgment.

How the Critical Audit Matter Was Addressed in the Audit

Our auditing procedures related to allowances for rebates for Epidiolex product sales included the following, among others:

- We tested the effectiveness of internal controls over the development of the allowances for rebates, including the underlying assumptions and key inputs into the Company's allowances for rebates as well as controls over management's review of the application of the governmental pricing regulations.
- We compared the significant assumptions used by management to currently available historical trends, evaluated the change in the accruals from prior periods, and assessed the historical accuracy of management's estimates against actual results.
- We estimated the rebates accrual for a sample of U.S. programs, using a combination of Company internal data, historical information, executed contracts, and third-party data and compared our estimate to the amount recorded by the Company.
- We tested the completeness and accuracy of the underlying data used in the Company's calculations through reconciliation to third-party invoices, executed contracts, claims data, and actual cash payments.

/s/ DELOITTE & TOUCHE LLP

San Diego, California
February 27, 2020

We have served as the Company's auditor since 2018.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of GW Pharmaceuticals plc

Opinion on the Financial Statements

We have audited the accompanying consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows of GW Pharmaceuticals plc and subsidiaries (the "Company"), for the year ended September 30, 2017, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the results of its operations and its cash flows for the year ended September 30, 2017, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audit. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audit, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audit included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ *DELOITTE LLP*

London, United Kingdom
November 28, 2018

We began serving as the Company's auditor in 2002. In 2018 we became the predecessor auditor.

GW PHARMACEUTICALS PLC
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)

	December 31, 2019	December 31, 2018
Assets		
Cash and cash equivalents	$ 536,933	$ 591,497
Accounts receivable, net	48,883	4,192
Inventory	85,528	33,030
Prepaid expenses and other current assets	28,292	17,903
Total current assets	699,636	646,622
Property, plant, and equipment, net	127,765	90,832
Operating lease assets	24,916	—
Goodwill	6,959	6,959
Deferred tax assets	18,123	8,720
Other assets	4,850	2,935
Total assets	$ 882,249	$ 756,068
Liabilities and stockholders' equity		
Accounts payable	$ 9,990	$ 9,796
Accrued liabilities	99,374	52,477
Current tax liabilities	437	2,384
Other current liabilities	7,760	1,559
Total current liabilities	117,561	66,216
Long-term liabilities:		
Finance lease liabilities	5,573	5,690
Operating lease liabilities	21,650	—
Other liabilities	11,431	10,082
Total long-term liabilities	38,654	15,772
Total liabilities	156,215	81,988
Commitments and contingencies (Note 10)		
Stockholders' equity:		
Ordinary shares par value £0.001; 371,068,436 and 366,616,688 shares outstanding as of December 31, 2019 and 2018, respectively	570	564
Additional paid-in capital	1,632,046	1,581,144
Accumulated deficit	(837,959)	(828,940)
Accumulated other comprehensive loss	(68,623)	(78,688)
Total stockholders' equity	726,034	674,080
Total liabilities and stockholders' equity	$ 882,249	$ 756,068

See accompanying notes to consolidated financial statements.

GW PHARMACEUTICALS PLC
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except per share amounts)

	Year Ended December 31, 2019	Three Months Ended December 31, 2018	Years Ended September 30, 2018	Years Ended September 30, 2017
Revenues				
Product net sales	$ 310,331	$ 6,617	$ 10,469	$ 7,957
Other revenue	1,001	37	2,268	672
Total revenues	311,332	6,654	12,737	8,629
Operating expenses				
Cost of product sales	27,199	1,829	5,986	4,521
Research and development	142,678	29,086	153,736	112,249
Selling, general and administrative	259,880	49,083	141,818	58,020
Total operating expenses	429,757	79,998	301,540	174,790
Loss from operations	(118,425)	(73,344)	(288,803)	(166,161)
Interest income	8,464	2,449	3,645	2,063
Interest expense	(1,087)	(295)	(1,249)	(951)
Other income	104,117	0	0	0
Foreign exchange loss	(2,272)	(982)	(4,963)	(6,442)
Loss before income taxes	(9,203)	(72,172)	(291,370)	(171,491)
Income tax (benefit) expense	(184)	(266)	3,797	(1,032)
Net loss	$ (9,019)	$ (71,906)	$ (295,167)	$ (170,459)
Net loss per common share, basic and diluted	$ (0.02)	$ (0.20)	$ (0.88)	$ (0.56)
Weighted average common shares outstanding, basic and diluted	371,580	366,458	333,936	305,826

See accompanying notes to consolidated financial statements.

GW PHARMACEUTICALS PLC
CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(in thousands)

	Year Ended December 31, 2019	Three Months Ended December 31, 2018	Years Ended September 30, 2018	Years Ended September 30, 2017
Net loss	$ (9,019)	$ (71,906)	$ (295,167)	$ (170,459)
Foreign currency translation adjustments	10,065	(3,494)	(676)	10,008
Comprehensive income (loss)	$ 1,046	$ (75,400)	$ (295,843)	$ (160,451)

See accompanying notes to consolidated financial statements.

GW PHARMACEUTICALS PLC
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31, 2019	Three Months Ended December 31, 2018	Years Ended September 30, 2018	Years Ended September 30, 2017
Cash flows from operating activities				
Net loss	$ (9,019)	$ (71,906)	$ (295,167)	$ (170,459)
Adjustments to reconcile net loss to net cash used in operating activities:				
Foreign exchange loss	2,709	742	4,917	9,280
Stock-based compensation	48,030	9,683	31,627	15,479
Depreciation and amortization	9,240	2,534	9,290	7,054
Deferred income taxes	(9,698)	(1,265)	(317)	(3,770)
Gain from sale of priority review voucher	(104,117)	—	—	—
Other	39	—	241	1,554
Changes in operating assets and liabilities:				
Accounts receivable, net	(44,623)	(2,125)	(804)	(277)
Inventory	(51,125)	(14,460)	(13,646)	5
Prepaid expenses and other current assets	(9,831)	(3,635)	14,489	(12,471)
Other assets	3,888	(47)	(564)	—
Accounts payable	805	(1,211)	2,238	3,171
Current tax liabilities	(963)	878	54	57
Accrued liabilities	43,110	5,942	16,507	1,253
Other liabilities	(1,914)	410	(733)	150
Net cash used in operating activities	(123,469)	(74,460)	(231,868)	(148,974)
Cash flows from investing activities				
Proceeds from sale of priority review voucher	104,117	—	—	—
Additions to property, plant and equipment	(40,386)	(18,687)	(31,362)	(19,285)
Additions to capitalized software	(2,102)	(63)	(2,042)	(812)
Proceeds from disposal of property, plant and equipment	—	—	517	—
Net cash provided by (used in) investing activities	61,629	(18,750)	(32,887)	(20,097)
Cash flows from financing activities				
Proceeds from issuance of ordinary shares, net of issuance costs	—	324,638	297,931	—
Proceeds from exercise of stock options	2,878	—	621	122
Payments on finance leases	(389)	(40)	(276)	(261)
Payments on landlord financing obligation	(543)	(130)	(522)	(1,074)
Net cash provided by (used in) financing activities	1,946	324,468	297,754	(1,213)
Effect of exchange rate changes on cash	5,330	5,326	(240)	8,993
Net increase (decrease) in cash and cash equivalents	(54,564)	236,584	32,759	(161,291)
Cash and cash equivalents at beginning of period	591,497	354,913	322,154	483,445
Cash and cash equivalents at end of period	$ 536,933	$ 591,497	$ 354,913	$ 322,154
Supplemental disclosure of cash flow information:				
Income taxes paid	$ 10,462	$ —	$ 3,726	$ 2,928
Interest paid	$ 1,087	$ 198	$ 1,249	$ 1,232
Supplemental disclosure of noncash information:				
Property and equipment purchases in accounts payable and accrued liabilities	$ 923	$ 1,899	$ 322	$ 1,793

See accompanying notes to consolidated financial statements.

GW PHARMACEUTICALS PLC
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)

	Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Loss	Equity
Balances at September 30, 2016	302,093	$ 479	$ 901,128	$ (291,408)	$ (84,526)	$ 525,673
Issuance of common stock from exercise of stock options	2,347	3	119	—	—	122
Net loss	—	—	—	(170,459)	—	(170,459)
Stock-based compensation	—	—	15,479	—	—	15,479
Other comprehensive income	—	—	—	—	10,008	10,008
Balances at September 30, 2017	304,440	$ 482	$ 916,726	$ (461,867)	$ (74,518)	$ 380,823
Issuance of common stock in public offering, net of issuance costs	33,120	44	297,888	—	—	297,932
Issuance of common stock from exercise of stock options	2,687	4	616	—	—	620
Net loss	—	—	—	(295,167)	—	(295,167)
Stock-based compensation	—	—	31,627	—	—	31,627
Other comprehensive loss	—	—	—	—	(676)	(676)
Balances at September 30, 2018	340,247	$ 530	$ 1,246,857	$ (757,034)	$ (75,194)	$ 415,159
Issuance of common stock in public offering, net of issuance costs	26,220	34	324,604	—	—	324,638
Issuance of common stock from exercise of stock options	150	—	—	—	—	—
Net loss	—	—	—	(71,906)	—	(71,906)
Stock-based compensation	—	—	9,683	—	—	9,683
Other comprehensive loss	—	—	—	—	(3,494)	(3,494)
Balances at December 31, 2018	366,617	$ 564	$ 1,581,144	$ (828,940)	$ (78,688)	$ 674,080
Issuance of common stock from exercise of stock options	4,452	6	2,872	—	—	2,878
Net loss	—	—	—	(9,019)	—	(9,019)
Stock-based compensation	—	—	48,030	—	—	48,030
Other comprehensive income	—	—	—	—	10,065	10,065
Balances at December 31, 2019	371,069	$ 570	$ 1,632,046	$ (837,959)	$ (68,623)	$ 726,034

See accompanying notes to consolidated financial statements.

Note 1: Business Overview

GW Pharmaceuticals plc and its subsidiaries (referred to herein as “we,” “us,” “our,” and the “Company”) is a biopharmaceutical company focused on discovering, developing and commercializing novel therapeutics from our proprietary cannabinoid product platform in a broad range of disease areas. The Company is developing a portfolio of cannabinoid medicines, of which the lead product is Epidiolex, an oral medicine for the treatment of certain refractory childhood epilepsies.

The Company is a public limited company, which has had American Depository Shares (ADSs) registered with the U.S. Securities and Exchange Commission (SEC) and has been listed on Nasdaq since May 1, 2013. Until December 5, 2016, the Company was also listed on the Alternative Investment Market, which is a submarket of the London Stock Exchange. The Company is incorporated and domiciled in the United Kingdom. The address of the Company’s registered office and principal place of business is Sovereign House, Vision Park, Histon, Cambridgeshire.

Note 2: Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany accounts and transactions have been eliminated in consolidation.

Change of Fiscal Year

We changed our fiscal year end to December 31 from September 30, effective December 31, 2018. This annual report is for the year ended December 31, 2019.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States (U.S. GAAP) requires management to make estimates and assumptions that affect the reported amounts in the consolidated financial statements and accompanying notes. Actual results could differ from these estimates.

Foreign Currency Translation

The financial position and results of operations of the Company’s non-U.S. subsidiaries are generally determined using local currency as the functional currency. Assets and liabilities of these subsidiaries are translated at the exchange rate in effect at each year end. Income statement accounts are translated at the average rate of exchange prevailing during the year. Adjustments arising from the use of differing exchange rates from period to period are included in accumulated other comprehensive loss in stockholders’ equity. Foreign currency transaction gains and losses are included in “foreign exchange loss” in the Company’s consolidated statements of operations.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity date of three months or less to be cash equivalents.

Fair Value of Financial Instruments

The carrying values of the Company’s financial instruments, consisting of cash and cash equivalents, trade receivables, interest and other receivables, and accounts payable and accrued liabilities, approximate fair value due to the relative short-term nature of these instruments.

Accounts Receivable

Accounts receivable are recorded net of customer allowances for prompt payment discounts, chargebacks, and doubtful accounts. Allowances for prompt payment discounts and chargebacks are based on contractual terms. The Company estimates the allowance for doubtful accounts based on existing contractual payment terms, actual payment patterns of its customers and individual customer circumstances. As of December 31, 2019, the allowance for doubtful accounts was $0.3 million. At December 31, 2018, the Company determined that an allowance for doubtful accounts was not required and no accounts were written off during the period.

Inventory

Inventory is stated at the lower of cost or estimated net realizable value. The Company uses a combination of standard and actual costing methodologies to determine the cost basis for its inventories which approximates actual cost. Inventory is valued on a first-in, first-out basis. The Company reduces its inventory to net realizable value for potentially excess, dated or obsolete inventory based on an analysis of forecasted demand compared to quantities on hand, as well as product shelf life.

Our inventory production process includes the cultivation of botanical raw material. Because of the duration of the cultivation process, a portion of our inventory will not be sold within one year. Consistent with the practice in other industries that cultivate botanical raw materials, all inventory is classified as a current asset.

The Company capitalizes inventory costs associated with its products upon regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed. Prior to FDA approval of Epidiolex, all costs related to the manufacturing of Epidiolex were charged to research and development expense in the period incurred.

Property, Plant, and Equipment

Property, plant, and equipment are recorded at cost and depreciated over their estimated useful lives using the straight-line method. Leasehold improvements are amortized over the shorter of their estimated useful lives or the term of the lease by use of the straight-line method. The estimated useful lives for buildings and leasehold improvements range from 4 to 20 years. The estimated useful lives of machinery and equipment range from 3 to 20 years. Construction-in-process reflects amounts incurred for property, equipment or improvements that have not been placed in service. Maintenance and repair costs are expensed as incurred. When assets are retired or sold, the assets and accumulated depreciation are removed from the respective accounts and any gain or loss is recognized.

Impairment of Long-Lived Assets

The Company reviews its long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by a comparison of the carrying amount of an asset to estimated future operating cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, an impairment charge is recognized by the amount by which the carrying amount of the asset exceeds the fair value of the asset.

Goodwill

Goodwill represents the excess of purchase price over fair value of net assets acquired in a business combination and is not amortized. Goodwill is subject to impairment testing at least annually or when a triggering event occurs that could indicate a potential impairment. We performed the annual assessment for goodwill impairment in December of 2019, noting no impairment.

Revenue Recognition

The Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Accounting Standards Codification (ASC) Topic 606, Revenue from Contracts with Customers (Topic 606), the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Revenue for the Company's product sales has not been adjusted for the effects of a financing component as the Company expects, at contract inception, that the period between when the Company's transfers control of the product and when the Company receives payment will be one year or less. Product shipping and handling costs are included in cost of product sales.

Epidiolex Product Net Sales

Epidiolex was approved by the FDA in June 2018. Subsequent to the approval by the FDA, the United States Drug Enforcement Agency (DEA) took action to change the classification of Epidiolex from a Schedule I controlled substance to a Schedule V controlled substance, thereby allowing Epidiolex to be prescribed and distributed in the United States. On November 1, 2018, the Company launched sales of Epidiolex to specialty pharmacies (SPs) and specialty distributors (SDs). The Company recognizes revenue from product sales upon receipt of product at the SPs and SDs, the date at which the control is transferred, net of the following allowances which are reflected either as a reduction to the related account receivable or as an accrued liability, depending on how the allowance is settled:

Distribution Fees: Distribution fees include distribution service fees paid to the SPs and SDs based on a contractually fixed percentage of the wholesale acquisition cost (WAC), and prompt payment discounts. Distribution fees are recorded as an offset to revenue based on contractual terms at the time revenue from the sale is recognized.

Rebates: Allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program and the Medicare Part D prescription drug benefit, and contractual rebates with commercial payers. Rebates are amounts owed after the final dispensing of the product to a benefit plan participant and are based upon contractual agreements or statutory requirements. The allowance for rebates is based on contracted or statutory discount rates and expected utilization by benefit plan participants. The Company's estimates for expected utilization of rebates is based on utilization data received from the SPs since product launch. Rebates are generally invoiced and paid in arrears so that the accrual balance consists of an estimate of the amount expected to be incurred for the current quarter's activity, plus an accrual balance for prior quarters' unpaid rebates. If actual future rebates vary from estimates, the Company may need to adjust prior period accruals, which would affect revenue in the period of adjustment.

Chargebacks: Chargebacks are discounts and fees that relate to contracts with government and other entities purchasing from the SDs at a discounted price. The SDs charge back to the Company the difference between the price initially paid by the SDs and the discounted price paid to the SDs by these entities. The Company also incurs group purchasing organization fees for transactions through certain purchasing organizations. The Company estimates sales with these entities and accrues for anticipated chargebacks and organization fees, based on the applicable contractual terms. If actual future chargebacks vary from these estimates, the Company may need to adjust prior period accruals, which would affect revenue in the period of adjustment.

Co-Payment Assistance: The Company offers co-payment assistance to commercially insured patients meeting certain eligibility requirements. Co-payment assistance is accrued for based on actual program participation and estimates of program redemption using data provided by third-party administrators.

Product Returns: Consistent with industry practice, the Company offers the SPs and SDs limited product return rights for damages, shipment errors, and expiring product, provided that the return is within a specified period around the product expiration date as set forth in the applicable individual distribution agreement. The Company does not allow product returns for product that has been dispensed to a patient. As the Company receives inventory reports from the SPs and SDs and has the ability to control the amount of product that is sold to the SPs and SDs, it is able to make a reasonable estimate of future potential product returns based on this on-hand channel inventory data and sell-through data obtained from the SPs and SDs. In arriving at its estimate, the Company also considers historical product returns, the underlying product demand, and industry data specific to the specialty pharmaceutical distribution industry.

On September 23, 2019, the Company announced that the European Commission (EC) approved the marketing authorization for Epidyolex™ (the trade name in Europe for Epidiolex) for use as adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome, in conjunction with clobazam, for patients two years of age and older. The Company recognizes revenue from product sales in Europe upon delivery of the product, which is the point at which control of the goods is transferred to the customer. The Company recognizes revenue net of standard discounts and allowances, which are reflected as accrued liabilities.

The Company also sells Epidiolex in certain markets outside of the United States under early access programs that enable patients to receive the product prior to regulatory approval. Revenue under early access programs is generally recognized when the product is delivered.

The total amount deducted from gross sales for the allowances described above for the year ended December 31, 2019 was $63.3 million.

Sativex Product Net Sales

Sales of Sativex are made outside of the United States for the treatment of spasticity due to multiple sclerosis, or MS, pursuant to license agreements with commercial partners. Under these license agreements, the Company sells fully labeled Sativex vials to its commercial partners for a contractually agreed price, which is generally based on percentages of the commercial partners' in-market net selling price charged to end customers. Product net sales revenue related to Sativex shipments to commercial license partners is recognized when shipped, at which point the customer obtains control of the product. The Company commercializes Sativex in Australia and New Zealand through a consignment relationship with a local distributor. Product net sales revenues related to Sativex sales in Australia and New Zealand are recognized when the product is sold through to the end customer.

Other Revenue

The Company's other revenue primarily consists of research and development fee revenue for services provided under a license agreement with Otsuka Pharmaceutical Co. Ltd (Otsuka) that was terminated in December 2017 and variable consideration milestone payments related to the Sativex license agreements.

The research and development fee revenue is recognized at the time the underlying services are performed.

The Sativex license agreements contain provisions for the Company to earn variable consideration in the form of regulatory milestone payments, sales-based milestone payments, and royalty payments. The Company has no further performance obligations related to the regulatory milestone payments and these amounts are recognized in accordance with Topic 606 when receipt of these payments becomes probable and there is no significant risk of revenue reversal. Revenue related to the sales-based milestone payments and product royalty payments are subject to the sales-based royalty exception under Topic 606 and is recognized when the underlying sales are made.

Research and Development Expenses

Research and development expenses are charged to operations as incurred. Research and development expenses include, among other things, internal and external costs associated with preclinical development, pre-commercialization manufacturing expenses, and clinical trials. The Company accrues for costs incurred as the services are being provided by monitoring the status of the trial or services provided and the invoices received from its external service providers. In the case of clinical trials, a portion of the estimated cost normally relates to the projected cost to treat a patient in the trials, and this cost is recognized based on the number of patients enrolled in the trial. As actual costs become known, the Company adjusts its accruals accordingly.

Research and development expense is presented net of reimbursements from reimbursable tax and expenditure credits from the U.K. government. The majority of the Company’s pipeline research, clinical trials management and the Epidiolex and Sativex chemistry and manufacturing controls development activities, which are generally carried out by a subsidiary in the U.K., are eligible for inclusion under the U.K tax and expenditure rebate schemes. For the year ended December 31, 2019, three months ended December 31, 2018 and years ended September 30, 2018 and 2017, the Company recorded $4.0 million, $0.8 million, $4.3 million, and $26.0 million, respectively, of U.K. tax and expenditure rebates as a component of research and development expense.

Concentration Risk

Financial instruments, which potentially subject the Company to concentrations of credit risk, principally consist of cash, cash equivalents, investment securities, and accounts receivable. The Company’s cash and cash equivalents balances are primarily in depository accounts at major financial institutions in accordance with the Company’s investment policy. The Company’s investment policy defines allowable investments and establishes guidelines relating to credit quality, diversification, and maturities of its investments to preserve principal and maintain liquidity. Further, the Company specifies credit quality standards for its customers that are designed to limit the Company’s credit exposure to any single party.

For the year ended December 31, 2019, the Company’s five largest customers represented approximately 85% of the Company’s product net sales and 86% of the Company’s accounts receivable balance as of December 31, 2019. For the three months ended December 31, 2018, the Company’s five largest customers represented approximately 71% of the Company’s product net sales and 75% of the Company’s accounts receivable balance as of December 31, 2018. For the years ended September 30, 2018 and 2017, product net sales consisted entirely of Sativex sales outside of the United States pursuant to license agreements with a small number of commercial partners.

Share-based Compensation

The Company recognizes share-based compensation expense for grants of stock options under the Company's Long-Term Incentive Plans to employees and non-employee members of the Company's board of directors based on the grant-date fair value of those awards. The grant-date fair value of an award is generally recognized as compensation expense over the award's requisite service period. Expense related to awards with graded vesting is generally recognized over the vesting period using the accelerated attribution method.

The Company uses the Black-Scholes model to compute the estimated fair value of stock option awards. Using this model, fair value is calculated based on assumptions with respect to (i) expected volatility of the Company's ADS price, (ii) the periods of time over which employees and members of the board of directors are expected to hold their options prior to exercise (expected lives), (iii) expected dividend yield on the ordinary shares, and (iv) risk-free interest rates. Share-based compensation expense also includes an estimate, which is made at the time of grant, of the number of awards that are expected to be forfeited. This estimate is revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Income Taxes

The Company recognizes deferred tax assets and liabilities for temporary differences between the financial reporting basis and the tax basis of the Company's assets and liabilities along with net operating loss and tax credit carryovers. The Company records a valuation allowance against its deferred tax assets to reduce the net carrying value to an amount that it believes is more likely than not to be realized. When the Company establishes or reduces the valuation allowance against its deferred tax assets, its provision for income taxes will increase or decrease, respectively, in the period such determination is made.

Valuation allowances against the Company’s deferred tax assets were $114.5 million and $101.6 million at December 31, 2019 and 2018, respectively. Changes in the valuation allowances are generally recognized in the provision for income taxes as a component of the estimated annual effective tax rate.

Uncertain tax positions, for which management's assessment is that there is more than a 50% probability of sustaining the position upon challenge by a taxing authority based upon its technical merits, are subjected to certain recognition and measurement criteria. The Company re-evaluates uncertain tax positions and considers various factors, including, but not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, and changes in facts or circumstances related to a tax position. The Company adjusts the level of the liability to reflect any subsequent changes in the relevant facts and circumstances surrounding the uncertain positions. The Company recognizes interest and penalties related to income tax matters in income tax expense.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common shares and common stock equivalents outstanding for the period determined using the treasury stock method. For purposes of this calculation, market-priced stock options are considered to be common stock equivalents but are not included in the calculations of diluted net loss per share for the periods presented as their effect would be anti-dilutive. Nominal strike-price options are considered common stock equivalents and are included in the calculation of basic weighted average shares outstanding once they have become vested. The Company incurred net losses for all periods presented and there were no reconciling items for potentially dilutive securities. More specifically, at December 31, 2019, December 31, 2018, and September 30, 2018, and 2017, options totaling approximately 11.8 million, 13.0 million, 13.0 million, and 9.9 million ordinary shares, respectively, were excluded from the calculation of diluted net loss per share as their effect would have been anti-dilutive.

Segment and Geographic Reporting

Management has determined that the Company operates in one business segment which is the discovery, development and commercialization of novel therapeutics from its proprietary cannabinoid product platform in a broad range of disease areas.

Revenues recorded in the year ended December 31, 2019, three months ended December 31, 2018, and years ended September 30, 2018, and 2017 were generated in the following geographical areas:

	Year Ended December 31, 2019	Three Months Ended December 31, 2018	Years Ended September 30, 2018	2017
		(in thousands)		
United Kingdom	2,550	220	1,761	1,758
United States	288,164	4,669	1,560	121
Europe	16,516	1,131	6,882	5,447
Other	4,102	634	2,534	1,303
Total revenues	$ 311,332	$ 6,654	$ 12,737	$ 8,629

Long-lived assets which include property, plant, and equipment were located as follows:

	December 31,	
	2019	2018
	(in thousands)	
United Kingdom	$ 123,207	$ 89,550
United States	4,558	1,282
Total long-lived assets	$ 127,765	$ 90,832

Recently Issued Accounting Standards

Accounting Standards Update (ASU) 2016-13, Measurement of Credit Losses on Financial Instruments:

In June 2016, the FASB issued ASU 2016-13, which amends the impairment model by requiring entities to use a forward-looking approach based on expected losses to estimate credit losses on certain types of financial instruments, including trade receivables and available-for-sale debt securities. This guidance is effective for annual reporting periods beginning after December 15, 2019, including interim periods. The Company is finalizing the credit loss calculations and does not expect the adoption of this standard to have a significant impact on the Company's consolidated financial statements.

ASU 2019-12, Income Taxes: Simplifying the Accounting for Income Taxes:

In December 2019, the FASB issued ASU No. 2019-12, Simplifying the Accounting for Income Taxes, as part of its initiative to reduce complexity in accounting standards. The amendments in the ASU are effective for fiscal years beginning after December 15, 2020, including interim periods therein. Early adoption of the standard is permitted, including adoption in interim or annual periods for which financial statements have not yet been issued. We have not early adopted this ASU for 2019. The ASU is currently not expected to have a material impact on our consolidated financial statements.

Recently Adopted Accounting Standards

ASU 2016-02, Leases:

On January 1, 2019, the Company adopted ASU 2016-02 using the modified retrospective method. This new accounting standard requires a lessee to recognize an asset and liability for most leases on its balance sheet. The Company elected the optional transition method that allowed for a cumulative-effect adjustment as of January 1, 2019 and did not restate previously reported results in the comparative periods. The Company also elected to adopt certain practical expedients allowed by the new standard, which among other things, allowed the Company to carry forward its historical lease classification.

As a result of adoption of the new standard, the Company recorded operating lease assets and liabilities of approximately $20.5 million and $21.1 million, respectively, as of January 1, 2019. The operating lease liability was determined based on the present value of the remaining minimum rental payments and the operating lease asset was determined based on the value of the lease liability, adjusted for existing deferred rent balances, which were previously included in other current liabilities and other liabilities. Accounting for the Company's finance leases remains substantially unchanged. As a result of the adoption of the new leasing accounting standard, the Company's build-to-suit asset has been reclassified to buildings and the build-to-suit financing obligation has been reclassified to finance lease obligation in the consolidated balance sheets. In addition, the adoption of this new accounting standard resulted in increased qualitative and quantitative disclosures regarding the amount, timing, and uncertainty of cash flows arising from leases. For further details, see Note 11, *Leases*. The adoption of the new standard did not materially impact the Company's consolidated results of operations or cash flows.

Note 3: Sativex License Agreements

The Company has entered into license agreements for Sativex with major pharmaceutical companies that provide the license partners with exclusive rights in a defined geographic territory to commercialize Sativex for all indications. The Company has retained the exclusive right to manufacture and supply Sativex to license partners on commercial supply terms for the duration of the commercial life of the product.

In 2007, the Company entered into an exclusive license agreement with Otsuka Pharmaceutical Co., Ltd. (Otsuka) for the development and commercialization of Sativex in the United States. In December 2017, the Company entered into a mutual termination agreement with Otsuka to return the rights to develop and commercialize Sativex in the United States to the Company. As part of the termination agreement, the Company agreed to pay Otsuka a contingent future milestone payment of $10 million if Sativex achieves FDA approval in the U.S. and a total of $30 million of potential sales-based milestones if U.S. sales of Sativex reach certain thresholds. As of December 31, 2019, no amounts have been accrued related to the contingent payments because it is not probable that the milestones will be achieved.

Note 4: Fair Value Measurements

At December 31, 2019 and December 31, 2018, the Company's cash equivalents consisted of money market funds, which are classified as Level 1 within the fair value hierarchy defined by authoritative guidance.

Securities classified as Level 1 are valued using quoted market prices. The Company does not hold any securities classified as Level 2, which are securities valued using inputs that are either directly or indirectly observable, or Level 3, which are securities valued using unobservable inputs. The Company has not transferred any investment securities between the classification levels.

Note 5: Composition of Certain Balance Sheet Captions:

Inventory consisted of the following:

	December 31,	
	2019	2018
	(in thousands)	
Raw materials	$ 1,976	$ 676
Work in process	78,547	28,709
Finished goods	5,005	3,645
	$ 85,528	$ 33,030

Property, plant and equipment, net, consisted of the following:

	December 31,	
	2019	2018
	(in thousands)	
Buildings	4,725	4,573
Machinery and equipment	36,323	32,598
Leasehold improvements	42,744	36,004
Office and IT equipment	3,837	2,481
Construction-in-process	78,485	44,546
	166,114	120,202
Accumulated depreciation	(38,349)	(29,370)
	$ 127,765	$ 90,832

Depreciation of property and equipment was $8.0 million, $2.2 million, $8.5 million, and $7.0 million, for the year ended December 31, 2019, three months ended December 31, 2018 and for the years ended September 30, 2018, and 2017, respectively. The Company did not retire any property, plant, or equipment in the year ended December 31, 2019 and three months ended December 31, 2018. During the years ended September 30, 2018 and 2017, the Company retired $0.5 million, $1.8 million, respectively, of fully depreciated property, plant and equipment.

Accrued liabilities consisted of the following:

	December 31,	
	2019	2018
	(in thousands)	
Accrued compensation and benefits	$ 25,469	$ 18,482
Accrued vendor fees	29,731	11,452
Clinical trial accruals	10,382	10,059
Accrued growing fees	3,818	2,717
Accrued sales rebates and discounts	22,995	628
Other	6,979	9,139
	$ 99,374	$ 52,477

Other current liabilities consisted of the following:

	December 31,	
	2019	2018
	(in thousands)	
Finance lease liabilities	$ 305	$ 400
Operating lease liabilities	5,902	—
Landlord financing	595	539
Other	958	620
	$ 7,760	$ 1,559

Other liabilities consisted of the following:

	December 31,	
	2019	2018
	(in thousands)	
Landlord financing obligation	$ 9,152	$ 9,434
Other	2,279	648
	$ 11,431	$ 10,082

Note 6: Stockholders' Equity

In October 2018, the Company completed a public offering of 2,185,000 ADSs listed on the Nasdaq Global Market, representing 26,220,000 ordinary shares of the Company, at a price of $158.00 per ADS. The net proceeds from this transaction after underwriting discounts and commissions were approximately $324.6 million.

In December 2017, the Company completed a public offering of 2,760,000 ADSs listed on the Nasdaq Global market, representing 33,120,000 ordinary shares of the Company, at a price of $115.00 per ADS. The net proceeds from this transaction after underwriting discounts and commissions were approximately $297.9 million.

Note 7: Share-Based Compensation

Stock Plans

In March 2008, the Company adopted the GW Pharmaceuticals plc Long-Term Incentive Plan (the 2008 LTIP Plan). Share based awards granted by the Company from March 2008 to March 2017 were granted under the 2008 LTIP Plan. On March 14, 2017, the Company adopted the GW Pharmaceuticals plc 2017 Long-Term Incentive Plan (the 2017 LTIP Plan). The 2017 LTIP plan authorizes the Company to issue up to an aggregate of 15.0 million ordinary shares, or 1.3 million ADSs, related to share-based awards to employees, non-employee directors and consultants. No grants under the 2017 LTIP Plan may be made after March 13, 2022. As of December 31, 2019, 10.3 million ordinary shares have been or may be issued pursuant to share-based awards that have been granted under the 2017 LTIP Plan.

The Company issues new ordinary shares and the commensurate number of ADS when share-based awards are exercised.

Provisions of Share-Based Awards

The Company issues nominal strike price stock options, which have an exercise price equal to the £0.001 par value per ordinary share of the Company's ordinary shares, to executive officers, employees and non-employee directors. The Company also issues market-priced options to executive officers and non-employee directors. Nominal strike priced options granted to U.S. residents prior to April 2017 contain short-term expiration provisions so the awards are compliant with provisions of IRS Code 409(a). Nominal strike price options granted to U.S. residents beginning in April 2017 are awarded in the form of RSU-style options that automatically exercise on the vesting date.

Substantially all of the share-based awards issued by the Company have service-based vesting conditions. Many awards also have non-market-based performance conditions, which must be achieved within the service-based vesting period for the awards to vest. These performance conditions are generally linked to operational, regulatory or strategic milestones and are designed to incentivize individual employees and advance the Company's progress towards its strategic objectives. Share-based awards that do not automatically exercise at vest date expire ten years from the date of grant.

Share-Based Award Activity

The following tables summarize the Company's stock option activity. The number of options, the weighted average grant date fair value per stock option, and the weighted average exercise price are all on a per ordinary shares basis. The Company's ADSs that are listed on the Nasdaq Global Market each represent twelve ordinary shares.

The following table summarizes the Company's nominal strike price stock option activity:

	Year Ended December 31, 2019		Three Months Ended December 31, 2018		Years Ended September 30, 2018		2017	
	Nominal Strike Price Options	Weighted Average Grant Date Fair Value	Nominal Strike Price Options	Weighted Average Grant Date Fair Value	Nominal Strike Price Options	Weighted Average Grant Date Fair Value	Nominal Strike Price Options	Weighted Average Grant Date Fair Value
	(in thousands, except weighted average grant date fair value)							
Outstanding, beginning of period	11,182	$ 8.44	11,240	$ 8.41	9,752	$ 7.90	9,182	$ 5.16
Granted	3,493	13.93	184	9.58	4,247	9.34	3,097	9.66
Exercised	(3,798)	5.43	(150)	7.36	(2,617)	7.21	(2,239)	3.21
Cancelled	(418)	11.69	(92)	8.61	(142)	9.37	(288)	6.69
Outstanding, end of period	10,459	$ 11.24	11,182	$ 8.44	11,240	$ 8.41	9,752	$ 7.90
Exercisable, end of period	1,434	$ 5.47	1,054	$ 3.65	1,136	$ 6.11	1,986	$ 4.52

The following table summarizes the Company's market-priced stock option activity:

	Year Ended December 31, 2019		Three Months Ended December 31, 2018		Years Ended September 30, 2018		2017	
	Market Strike Price Options	Weighted Average Exercise Price	Market Strike Price Options	Weighted Average Exercise Price	Market Strike Price Options	Weighted Average Exercise Price	Market Strike Price Options	Weighted Average Exercise Price
	(in thousands, except weighted average grant date fair value)							
Outstanding, beginning of period	2,889	$ 8.49	2,889	$ 8.49	2,174	$ 8.28	1,452	$ 5.80
Granted	602	14.82	—	—	785	9.65	830	9.62
Exercised	(654)	2.32	—	—	(70)	9.03	(108)	1.15
Cancelled	(1)	3.89	—	—	—	—	—	—
Outstanding, end of period	2,836	$ 9.60	2,889	$ 8.49	2,889	$ 8.49	2,174	$ 8.28
Exercisable, end of period	620	$ 4.99	461	$ 6.90	257	$ 8.74	—	—

The weighted average per share fair value of market priced options granted during the year ended December 31, 2019 and years ended September 30, 2017 and 2018 was $14.82, $5.98, and $6.00, respectively. No market priced options were granted in the three months ended December 31, 2018.

The aggregate intrinsic value of the stock options exercised in the year ended December 31, 2019 was $52.9 million. The aggregate intrinsic value of the stock options exercised in the three months ended December 31, 2018 was $1.6 million. The aggregate intrinsic value of stock options exercised in the years ended September 30, 2018, and 2017 was $30.7 million and $22.9 million, respectively. As of December 31, 2019, the weighted average remaining contractual life of options outstanding and options exercisable are 4.6 years and 4.3 years, respectively. Based on the Company's closing year-end stock price of $102.01 per ADS (or $8.50 per ordinary share) at December 31, 2019, the aggregate intrinsic value of options outstanding and options exercisable are $92.2 million and $12.5 million, respectively.

Valuation and Expense Recognition of Share-Based Awards

The fair value of stock option awards that do not contain a market condition is estimated using the Black-Scholes option-pricing model. The estimated fair value of each stock option is then expensed over the requisite service period, which is generally the vesting period. The determination of fair value using the Black-Scholes model is affected by the Company's ADS price as well as assumptions regarding a number of complex and subjective variables, including expected ADS price volatility, risk-free interest rate, expected dividends and projected employee stock option exercise behaviors. Stock options granted during the year ended December 31, 2019, three months ended December 31, 2018 and the years ended September 30, 2018 and 2017 were valued using the Black-Scholes option-pricing model with the following weighted-average assumptions:

	Year Ended December 31,	Three Months Ended December 31,	Years Ended September 30,	
	2019	2018	2018	2017
Expected volatility	56%	58%	63%	69%
Risk-free interest rate	2.56%	2.70%	2.30%	1.93%
Expected dividend yield	0%	0%	0%	0%
Expected life of options in years	6.50	6.50	6.50	6.50

The Company estimates its stock price volatility based using a combination of historical stock price volatility and the average implied volatility of options traded in the open market. The risk-free interest rate assumption is based on observed interest rates for the appropriate term of the Company's stock options. The Company has never declared or paid dividends and has no plans to do so in the foreseeable future. The expected option life assumption is estimated using the simplified method prescribed by ASC 718 and is based on the mid-point between vest date and expiration date since the Company does not have sufficient exercise history to estimate expected option life of historical grants.

Compensation expense for share-based awards based on a service condition is recognized only for those awards that are ultimately expected to vest. An estimated forfeiture rate has been applied to unvested awards for the purpose of calculating compensation cost. Forfeitures were estimated based on historical experience. These estimates are revised, if necessary, in future periods if actual forfeitures differ from the estimates. Changes in forfeiture estimates impact compensation cost in the period in which the change in estimate occurs. Compensation expense for share-based awards with graded, service-based vesting conditions is recognized over the requisite service period using the accelerated attribution method.

The table below summarizes the total share-based compensation expense included in the Company's statements of operations for the periods presented:

	Year Ended December 31,	Three Months Ended December 31,	Years Ended September 30,	
	2019	2018	2018	2017
		(in thousands)		
Research and development	$ 9,757	$ 6,887	$ 9,385	$ 5,239
Sales, general and administrative	35,468	2,382	22,242	10,240
	45,225	$ 9,269	$ 31,627	$ 15,479

For the year ended December 31, 2019, $2.8 million of share-based compensation related to manufacturing operations was capitalized into inventory. For the three months ended December 31, 2018, $0.4 million of share-based compensation related to manufacturing operations was capitalized into inventory. Share-based compensation related to manufacturing operations capitalized into inventory for the years ended September 30, 2018 and 2017 were negligible.

As of December 31, 2019, total compensation cost related to non-vested stock options not yet recognized was approximately $45.2 million, which is expected to be recognized over the next 42 months (10 months on a weighted average basis).

Note 8: Retirement Plans

The Company operates defined contribution retirement plans in the U.S. and U.K. for the benefit of all qualifying employees. The Company makes discretionary contributions to these plans and contributed $4.6 million, $0.9 million, $3.3 million, and $2.5 million in the year ended December 31, 2019, three months ended December 31, 2018 and years ended September 30, 2018 and 2017, respectively.

Note 9: Income Taxes

Income (loss) before income taxes is as follows:

	Year Ended December 31,	Three Months Ended December 31,	Years Ended September 30,	
	2019	2018	2018	2017
		(in thousands)		
United States	$ 22,822	$ 1,487	$ 12,041	$ 3,725
United Kingdom	(32,025)	(73,659)	(303,411)	(175,216)
	$ (9,203)	$ (72,172)	$ (291,370)	$ (171,491)

The components of income tax (benefit) expense are as follows:

	Year Ended December 31,	Three Months Ended December 31,	Years Ended September 30,	
	2019	2018	2018	2017
		(in thousands)		
Current				
U.S. federal	$ 7,397	$ 945	$ 3,885	$ 2,676
U.S. state and local	2,117	54	229	62
United Kingdom	—	—	—	—
Total Current	$ 9,514	$ 999	$ 4,114	$ 2,738
Deferred				
U.S. federal	$ (6,372)	$ (1,166)	$ (263)	$ (3,685)
U.S. state and local	(3,326)	(99)	(54)	(85)
United Kingdom	—	—	—	—
Total Deferred	$ (9,698)	$ (1,265)	$ (317)	$ (3,770)
Total income tax (benefit) expense	$ (184)	$ (266)	$ 3,797	$ (1,032)

As of December 31, 2019, December 31, 2018, September 30, 2018, and September 30, 2017, respectively, the tax effects of temporary differences and carryforwards that give rise to deferred tax assets and liabilities were as follows:

	Year Ended December 31,	Three Months Ended December 31,	Years Ended September 30,	
	2019	2018	2018	2017
	(in thousands)			
Deferred tax assets:				
Net operating losses	$ 106,421	$ 94,999	$ 94,570	$ 46,379
Research and development tax credits	668	180	180	506
Share-based compensation	14,515	10,057	8,745	7,496
Accrued expenses	3,268	2,275	2,320	1,787
Capitalized costs	1,688	3,219	—	—
Operating lease liabilities	1,837	—	—	—
Rebates and allowances	5,172	136	—	—
Depreciation	279	—	—	—
Other	428	689	291	199
Total gross deferred tax assets, net of valuation allowance	134,276	111,555	106,106	56,367
Valuation allowance	(114,525)	(101,606)	(97,462)	(46,126)
	19,751	9,949	8,644	10,241
Deferred tax liabilities:				
Depreciation	—	$ (1,229)	$ (1,310)	$ (2,220)
Operating lease assets	(1,628)	—	—	—
Deferred revenue	—	—	—	(1,216)
Total gross deferred tax liabilities	(1,628)	(1,229)	(1,310)	(3,436)
Net of deferred tax assets and liabilities	$ 18,123	$ 8,720	$ 7,334	$ 6,805

A valuation allowance of $114.5 million, $101.6 million, $97.5 million, and $46.1 million at December 31, 2019, December 31, 2018, September 30, 2018 and 2017, respectively, has been recognized to offset net deferred tax assets where realization of such assets is uncertain. The valuation allowances are primarily related to deferred tax assets for operating loss carryforwards and temporary differences related to share-based compensation expense of the Company’s U.K. operations.

The following table reconciles the Company's effective tax rate to the United Kingdom statutory rate:

	Year Ended December 31,	Three Months Ended December 31,	Years Ended September 30,	
	2019	2018	2018	2017
Tax, computed at the U.K. statutory rate	19.0%	19.0%	19.0%	19.5%
Non-deductible expenses	(5.2%)	(0.2%)	(0.1%)	(0.6%)
U.S. research tax credits, net	39.3%	0.4%	0.9%	1.6%
Surrender of R&D expenditures for U.K. research tax credits, net	(1.9%)	—	(0.1%)	(5.7%)
Foreign Derived Intangible Income	6.8%	0.8%	—	—
Share-based compensation	61.2%	0.2%	0.9%	2.1%
Changes in valuation allowances	(96.2%)	(19.6%)	(20.5%)	(16.2%)
State rate change	13.5%	—	—	—
Current/Deferred tax rate differential	(21.4%)	—	—	—
Overseas profits taxed at different rates	(13.9%)	(0.1%)	(0.3%)	—
Remeasurement of deferred taxes from 2017 Tax Act	0.0%	—	(1.0%)	—
Other	0.8%	(0.1%)	(0.1%)	(0.1%)
Effective income tax rate	2.0%	0.4%	(1.3%)	0.6%

The Company is headquartered in the United Kingdom and has subsidiaries in the United Kingdom, United States, Europe, and Australia.

The Company incurs tax losses in the United Kingdom. The weighted-average U.K. corporate tax rate for the year ended December 31, 2019, three months ended December 31, 2018, and years ended September 30, 2018, and 2017 was 19.0%, 19.0%, 19.0%, and 19.5%, respectively. The United Kingdom's 2016 Finance Bill, which was enacted on September 15, 2016, contained reductions in corporation tax to 19% from April 1, 2017 and 17% from April 1, 2020. The Company used a 17% tax rate as of December 31, 2019 in respect of the measurement of deferred taxes arising in the United Kingdom, which reflects the currently enacted tax rate based upon the anticipated timing of the unwinding of the deferred tax balances.

As of December 31, 2019, the Company had U.K. net operating loss carryforwards of approximately $626.0 million. Unsurrendered U.K. tax losses and tax credit carryforwards can be carried forward indefinitely to be offset against future taxable profits, however this is restricted to an annual £5 million allowance in each standalone company or group and above this allowance, there will be a 50% restriction in the profits that can be covered by losses brought forward.

The Company's subsidiary in the United States has generated taxable profits due to the commercialization of Epidiolex in the United States and service agreements between the Company's subsidiaries in the United States and the United Kingdom. The U.S. federal corporate tax rate for the year ended December 31, 2019, three months ended December 31, 2018, and years ended September 30, 2018 and 2017 was 21.0%, 21.0%, 24.5%, and 35%, respectively. The U.S. federal statutory tax rate has decreased due to U.S. tax reform which was enacted in December 2017.

The impact of income taxes outside of the United States and United Kingdom are not significant.

The Company's tax returns are subject to examination in the U.K. and U.S. The Company is no longer subject to examinations by tax authorities for tax years ended September 30, 2017 and prior in the United Kingdom. The Company's U.K. income tax returns have been submitted to Her Majesty's Revenue and Customs through the period ended December 31, 2018 and may be subject to audit until December 31, 2020. The Company is subject to examinations by U.S. Federal tax authorities for tax years ended December 31, 2018 and September 30, 2018, 2017, and 2016, and by state authorities for the tax years ended December 31, 2018 and September 30, 2018, 2017, 2016, and 2015. The California Franchise Tax Board has initiated an income tax audit of the Company's U.S. subsidiary for tax years ended September 30, 2017, 2016, and 2015.

Unrecognized tax benefits arise when the estimated benefit recorded in the financial statements differs from the amounts taken or expected to be taken in a tax return because of the uncertainties described above. The Company's total amount of unrecognized tax benefits was $2.4 million, $1.9 million, $1.8 million, and $1.1 million as of December 31, 2019, December 31, 2018, September 30, 2018 and 2017, respectively. The Company's policy is to recognize interest and penalties related to uncertain tax positions as a component of income tax expense and unrecognized tax benefits. The amounts accrued for interest and penalty charges as of December 31, 2019, December 31, 2018, September 30, 2018 and 2017 were not significant. If recognized, $2.4 million would affect the effective tax rate. The Company does not anticipate that the amount of unrecognized tax benefits as of December 31, 2019 will significantly change within the next twelve months.

The reconciliation of the beginning and ending amount of unrecognized tax benefits was as follows:

	Year Ended December 31, 2019	Three Months Ended December 31, 2018	Years Ended September 30, 2018	2017
		(in thousands)		
Balance, beginning of period	$ 1,943	$ 1,826	$ 1,134	$ 884
Additions for tax positions related to current year	416	34	771	453
Additions for tax positions related to prior years	32	83	46	18
Reduction for tax positions related to prior years	—	—	(125)	(221)
Balance, end of period	$ 2,391	$ 1,943	$ 1,826	$ 1,134

Note 10: Commitments and Contingencies

Landlord Financing

In 2013, the Company entered into an agreement with its landlord for the construction of a new production facility. In conjunction with agreement, the Company's landlord provided $13.1 million of funding to the Company for the internal fit out of the production facility. The repayment of this landlord financing takes the form of quarterly rent payments over a 15-year period that commenced in May 2016. The landlord financing liability is accounted for at amortized cost using the effective interest method at a rate of 7.0%. As of December 31, 2019 and 2018, the total landlord financing liability balance was $9.7 million and $10.0 million, respectively and included in "other current liabilities" and "other liabilities" in the Company's consolidated balance sheets.

Legal Proceedings

As of December 31, 2019, the Company was not a party to any material legal proceedings. The Company is not aware of any other proceedings or claims that it believes will have, individually or in the aggregate, a material adverse effect on its business, financial condition or results of operations.

Note 11: Leases

The Company leases buildings, land, equipment, and automobiles. Additionally, the Company has growing and cultivation contracts that contain embedded facility leases. The Company determines if an arrangement is a lease or contains a lease at contract inception. For contracts that are or contain leases, the Company records right-of-use (ROU) lease assets and lease liabilities at lease commencement based on the present value of lease payments over the lease term. The lease term includes renewal option periods when those options are reasonably certain to be exercised. The present value of lease payments is calculated using the Company's incremental collateralized borrowing rate unless an implicit rate is readily determinable. ROU lease assets include any upfront payments and exclude lease incentives. The Company accounts for lease and non-lease components as a single lease component for all of its leases except embedded leases, for which the lease and non-lease components are accounted for separately.

Leases are classified at lease commencement as either operating leases or finance leases. Operating lease assets are included in non-current assets and operating lease liabilities are included in other current liabilities and operating lease liabilities in our consolidated balance sheets. Operating lease cost is recognized on a straight-line basis over the lease term. Finance lease assets are included in property, plant and equipment, net, and finance lease liabilities are included in other current liabilities and finance lease liabilities in our consolidated balance sheets. Finance lease cost is recognized as depreciation expense of fixed assets and interest expense on finance lease liabilities. Leases with an initial term of 12 months or less are not recorded in the consolidated balance sheets and expense for these leases is recognized on a straight-line basis over the lease term.

The Company's lease costs consist of the following:

	Year Ended December 31, 2019
	(in thousands)
Lease cost	
Operating lease cost (1)	$ 7,446
Finance lease cost	
Amortization of leased assets	383
Interest on lease liabilities	403
Total lease cost	$ 8,232

(1) Includes short-term lease expense and variable cost, which are immaterial.

For the year ended December 31, 2019, approximately $2.7 million of operating and finance lease cost related to manufacturing operations was capitalized into inventory.

The following table summarizes cash flow information related to the Company's lease obligations:

	Year Ended December 31, 2019
	(in thousands)
Operating cash used for operating leases	$ 7,081
Operating cash used for finance leases	$ 403
Financing cash used for finance leases	$ 389

In the year ended December 31, 2019, $7.6 million of operating lease assets were exchanged for lease liabilities related to newly commenced leases.

The following table summarizes the Company's lease assets and liabilities:

	As of December 31, 2019
	(in thousands)
Lease assets	
Operating lease assets	$ 24,916
Finance lease assets	5,571
Total lease assets	$ 30,487
Lease liabilities	
Current	
Operating lease liabilities	5,902
Finance lease liabilities	305
Non-current	
Operating lease liabilities	21,650
Finance lease liabilities	5,573
Total lease liabilities	$ 33,430

The following table summarizes other supplemental information related to the Company's lease obligations:

	As of December 31, 2019
Weighted average remaining lease term (years)	
Operating leases	7.2
Finance leases	14.2
Weighted average discount rate	
Operating leases	5.5%
Finance leases	7.6%

The Company's future minimum annual lease payments under operating and finance leases as of December 31, 2019 are as follows:

	Operating Leases	Finance Leases
	(in thousands)	
2020	5,900	729
2021	5,498	729
2022	4,599	721
2023	3,782	718
2024	3,701	718
Thereafter	11,437	6,173
Total lease payments	$ 34,917	$ 9,788
Future cash lease incentives	746	—
Less amounts representing interest	6,619	3,910
Total lease obligations	$ 27,552	$ 5,878

Prior to January 1, 2019, the Company accounted for leases under the previous U.S. GAAP lease guidance, Accounting Standards Codification Topic 840, Leases. Rent expense for operating leases was $1.8 million and $5.7 million for the three months ended December 31, 2018 and year ended September 30, 2018, respectively. The aggregate future minimum rent payments under leases in effect as of December 31, 2018 were $6.4 million in 2019, $6.9 million in 2020, $5.7 million in 2021, $4.2 million in 2022, $2.8 million in 2023, and $11.8 million thereafter.

Note 12: Sale of Priority Review Voucher

In April 2019, the Company sold the rare pediatric disease PRV it received from the FDA in connection with the United States approval of Epidiolex to Biohaven Pharmaceutical Holding Ltd. for consideration of $105.0 million. The net proceeds of $104.1 million from the sale of the PRV was recognized as a gain on the sale of an intangible asset within other income on the consolidated statements of operations, as the PRV did not have a carrying value on the Company's consolidated balance sheet at the time of sale.

Note 13: Financial Statements and Supplementary Data (Unaudited)

The following interim financial information reflects all normal recurring adjustments necessary to fairly present the Company's quarterly financial results. The summarized quarterly data for the year ended December 31, 2019, three months ended December 31, 2018, and year ended September 30, 2018 are as follows:

	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
	(in thousands, except share and per share amounts)			
Revenue	$ 39,247	$ 72,038	$ 90,971	$ 109,076
Operating loss	(51,337)	(29,322)	(17,658)	(20,108)
Net (loss) income attributable to ordinary shareholders	(50,064)	79,748	(13,757)	(24,946)
Net (loss) income per ordinary share, basic	(0.14)	0.21	(0.04)	(0.07)
Net (loss) income per ordinary share, diluted	(0.14)	0.21	(0.04)	(0.07)
Weighted average shares outstanding, basic	369,823	371,712	372,246	372,447
Weighted average shares outstanding, diluted	369,823	377,435	372,246	372,447

	December 31, 2017	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
	(in thousands, except share and per share amounts)				
Revenue	$ 3,992	$ 3,041	$ 3,284	$ 2,420	$ 6,654
Operating loss	(58,548)	(68,242)	(81,406)	(80,607)	(73,344)
Net loss attributable to ordinary shareholders	(61,816)	(69,461)	(84,011)	(79,879)	(71,906)
Net loss per ordinary share, basic and diluted	(0.20)	(0.20)	(0.25)	(0.23)	(0.20)
Weighted average shares outstanding, basic and diluted	313,730	340,252	340,457	341,302	366,458

Note 14: Transition Period

The Company is presenting audited financial statements for the three months ended December 31, 2018. The following tables provide certain unaudited comparative financial information for the same period of the prior year.

	Three Months Ended December 31,	
	2018	2017
	(in thousands, except share and per share amounts)	
Revenues		
Product net sales	$ 6,617	$ 2,220
Other revenue	37	1,772
Total revenues	6,654	3,992
Operating expenses		
Cost of product sales	1,829	1,171
Research and development	29,086	36,195
Selling, general and administrative	49,083	25,174
Total operating expenses	79,998	62,540
Loss from operations	(73,344)	(58,548)
Interest income	2,449	604
Interest expense	(295)	(314)
Foreign exchange (loss) gain	(982)	160
Loss before income taxes	(72,172)	(58,098)
Income tax (benefit) expense	(266)	3,718
Net loss	$ (71,906)	$ (61,816)
Net loss per common share, basic and diluted	$ (0.20)	$ (0.20)
Weighted average common shares outstanding, basic and diluted	366,458	313,730

	Three Months Ended December 31,	
	2018	2017
	(in thousands)	
Cash flows from operating activities		
Net loss	$ (71,906)	$ (61,816)
Adjustments to reconcile net loss to net cash used in operating activities:		
Foreign exchange loss (gain)	742	(180)
Stock-based compensation	9,683	5,592
Depreciation and amortization	2,534	2,163
Deferred income taxes	(1,265)	(1,152)
Other	—	8
Changes in operating assets and liabilities:		
Accounts receivable, net	(2,125)	(223)
Inventory	(14,460)	378
Prepaid expenses and other current assets	(3,635)	(516)
Other assets	(47)	(166)
Accounts payable	(1,211)	(1,802)
Current tax liabilities	878	4,898
Accrued liabilities	5,942	3,004
Other current liabilities	93	(2,071)
Long-term liabilities	317	325
Net cash used in operating activities	(74,460)	(51,558)
Cash flows from investing activities		
Additions to property, plant and equipment	(18,687)	(7,748)
Additions to capitalized software	(63)	(993)
Proceeds from disposal of property, plant and equipment	—	—
Net cash used in investing activities	(18,750)	(8,741)
Cash flows from financing activities		
Proceeds from issuance of ordinary shares, net of issuance costs	324,638	297,932
Proceeds from exercise of stock options	—	1
Payments on build-to-suit financing obligation	—	(26)
Payments on capital leases	(40)	(39)
Payments on landlord financing obligation	(130)	(125)
Net cash provided by (used in) financing activities	324,468	297,743
Effect of exchange rate changes on cash	5,326	(371)
Net increase (decrease) in cash and cash equivalents	236,584	237,073
Cash and cash equivalents at beginning of period	354,913	322,154
Cash and cash equivalents at end of period	$ 591,497	$ 559,227

Exhibit 4.4

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

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

We have appointed Citibank as depositary bank pursuant to a deposit agreement. A copy of the deposit agreement is on file with the SEC under cover of a Registration Statement on Form F-6. A copy of the deposit agreement is available from the SEC's website (www.sec.gov). Please refer to Registration Number 333-187978 when retrieving such copy.

"Holder" means the person or persons in whose name an ADS is registered on the register maintained by the Depositary for such purpose.

Each ADS represents the right to receive 12 ordinary shares, each of which is frequently referred to as a "Share" or collectively, as "Shares", on deposit with the custodian. An ADS also represents the right to receive any other property received by the depositary bank or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. The custodian, the depositary bank and their respective nominees will hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depositary bank, the custodian or their nominees. Beneficial ownership in the deposited property will under the terms of the deposit agreement be vested in the beneficial owners of the ADSs. The depositary bank, the custodian and their respective nominees will be the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. Owners of ADSs will be able to exercise beneficial ownership interests in the deposited property only through the registered holders of the ADSs, by the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depositary bank, and by the depositary bank (on behalf of the owners of the corresponding ADSs) directly, or indirectly through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.

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

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with such reporting requirements and obtaining such approvals. Neither the depositary bank, the custodian, us nor any of their or our respective agents or affiliates shall be required to take any actions whatsoever on your behalf to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depositary bank will hold on your behalf the shareholder rights attached to the Shares underlying your ADSs. As an owner of ADSs you will be able to exercise the shareholders rights for the Shares represented by your ADSs through the depositary bank only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.

Dividends and Distributions

Holders generally have the right to receive the distributions we make on the securities deposited with the custodian. A Holder's receipt of these distributions may be limited, however, by practical considerations and legal limitations. Holders will receive such distributions under the terms of the deposit agreement in proportion to the number of ADSs held as of the specified record date, after deduction of the applicable fees, taxes and expenses.

Distributions of Cash

Whenever we make a cash distribution for the securities on deposit with the custodian, we will deposit the funds with the custodian. Upon receipt of confirmation of the deposit of the requisite funds, the depositary bank will arrange for the funds to be converted into U.S. dollars and for the distribution of the U.S. dollars to the holders, subject to the laws and regulations of England and Wales.

The conversion into U.S. dollars will take place only if practicable and if the U.S. dollars are transferable to the United States. The depositary bank will apply the same method for distributing the proceeds of the sale of any property (such as undistributed rights) held by the custodian in respect of securities on deposit.

The distribution of cash will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. The depositary bank will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable holders and beneficial owners of ADSs until the distribution can be effected or the funds that the depositary bank holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States.

Distributions of Shares

Whenever we make a free distribution of ordinary shares for the securities on deposit with the custodian, we will deposit the applicable number of ordinary shares with the custodian. Upon receipt of confirmation of such deposit, the depositary bank will *either* distribute to holders new ADSs representing the ordinary shares deposited *or* modify the ADS-to-ordinary share ratio, in which case each ADS a Holder holds will represent rights and interests in an integral number of the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-ordinary share ratio upon a distribution of ordinary shares will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depositary bank may sell all or a portion of the new ordinary shares so distributed.

No such distribution of new ADSs will be made if it would violate a law (i.e., the U.S. securities laws) or if it is not practicable. If the depositary bank does not distribute new ADSs as described above, it may sell the ordinary shares received upon the terms described in the deposit agreement and will distribute the proceeds of the sale as in the case of a distribution of cash.

Distributions of Rights

Whenever we intend to distribute rights to purchase additional ordinary shares, we will give prior notice to the depositary bank and will indicate whether we wish the elective distribution to be made available to you. In such case, we will assist the depositary bank in determining whether such distribution is lawful and reasonably practicable to distribute rights to purchase additional ADSs to holders.

The depositary bank will establish procedures to distribute rights to purchase additional ADSs to holders and to enable such holders to exercise such rights if it is lawful and reasonably practicable to make the rights available to holders of ADSs, we indicate that we wish such rights to be made available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement (such as opinions to address the lawfulness of the transaction). A Holder may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs upon the exercise of a Holder's rights. The depositary bank is not obligated to establish procedures to facilitate the distribution and exercise by holders of rights to purchase new ordinary shares other than in the form of ADSs.

The depositary bank will *not* distribute the rights to a Holder if:

- We do not timely request that the rights be distributed to a Holder or we request that the rights not be distributed to a Holder; or
- We fail to deliver satisfactory documents to the depositary bank; or
- It is not reasonably practicable to distribute the rights.

The depositary bank will sell the rights that are not exercised or not distributed if such sale is lawful and reasonably practicable. The proceeds of such sale will be distributed to holders as in the case of a cash distribution. If the depositary bank is unable to sell the rights, it will allow the rights to lapse.

Elective Distributions

Whenever we intend to distribute a dividend payable at the election of shareholders either in cash or in additional shares, we will give prior notice thereof to the depositary bank and will indicate whether we wish the elective distribution to be made available to a Holder. In such case, we will assist the depositary bank in determining whether such distribution is lawful and reasonably practicable.

The depositary bank will make the election available to a Holder only if it is lawful and reasonably practicable, we indicate that we wish such election to be made available to holders of ADSs, and if we have provided all of the documentation contemplated in the deposit agreement. In such case, the depositary bank will establish procedures to enable a Holder to elect to receive either cash or additional ADSs, in each case as described in the deposit agreement.

If the election is not made available to a Holder, such Holder will receive either cash or additional ADSs, upon the terms described above for distributions of cash and ordinary shares, respectively, depending on what a shareholder in England and Wales would receive upon failing to make an election, as more fully described in the deposit agreement.

Other Distributions

Whenever we intend to distribute property other than cash, ordinary shares or rights to purchase additional ordinary shares, we will notify the depositary bank in advance and will indicate whether we wish such distribution to be made to Holders. If so, we will assist the depositary bank in determining whether such distribution to holders is lawful and reasonably practicable.

If it is reasonably practicable to distribute such property to a Holder, we indicate that we wish such distribution to be made available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement, the depositary bank will distribute the property to the holders in a manner it deems practicable.

The distribution will be made net of fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes and governmental charges, the depositary bank may sell all or a portion of the property received.

The depositary bank will *not* distribute the property to a Holder and will sell the property if:

- We do not request that the property be distributed to a Holder or if we ask that the property not be distributed to a Holder; or
- We do not deliver satisfactory documents to the depositary bank; or
- The depositary bank determines that all or a portion of the distribution to a Holder is not reasonably practicable.

The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

Redemption

Whenever we decide to redeem any of the securities on deposit with the custodian, we will notify the depositary bank in advance. If it is practicable and if we provide all of the documentation contemplated in the deposit agreement, the depositary bank will provide notice of the redemption to the holders.

The custodian will be instructed to surrender the shares being redeemed against payment of the applicable redemption price. The depositary bank will convert the redemption funds received into U.S. dollars upon the terms of the deposit agreement and will establish procedures to enable holders to receive the net proceeds from the redemption upon surrender of their ADSs to the depositary bank. A Holder may have to pay fees, expenses, taxes and other governmental charges upon the redemption of a Holder's ADSs. If less than all ADSs are being redeemed, the ADSs to be retired will be selected by lot or on a *pro rata* basis, as the depositary bank may determine.

Changes Affecting Ordinary Shares

The ordinary shares held on deposit for a Holder's ADSs may change from time to time. For example, there may be a change in nominal or par value, a split-up, cancellation, consolidation or any other reclassification of such ordinary shares or a recapitalization, reorganization, merger, consolidation or sale of assets of the Company.

If any such change were to occur, a Holder's ADSs would, to the extent permitted by law, represent the right to receive the property received or exchanged in respect of the ordinary shares held on deposit. The depositary bank may in such circumstances deliver new ADSs to a Holder, amend the deposit agreement, the ADRs and the applicable Registration Statement(s) on Form F-6, call for the exchange of a Holder's existing ADSs for new ADSs and take any other actions that are appropriate to reflect as to the ADSs the change affecting the Shares. If the depositary bank may not lawfully distribute such property to a Holder, the depositary bank may sell such property and distribute the net proceeds to a Holder as in the case of a cash distribution.

Issuance of ADSs upon Deposit of Ordinary Shares

The depositary bank may create ADSs on a Holder's behalf if a Holder or a Holder's broker deposit ordinary shares with the custodian. The depositary bank will deliver these ADSs to the person a Holder indicates only after a Holder pays any applicable issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian. A Holder's ability to deposit ordinary shares and receive ADSs may be limited by U.S. and English legal considerations applicable at the time of deposit.

The issuance of ADSs may be delayed until the depositary bank or the custodian receives confirmation that all required approvals have been given and that the ordinary shares have been duly transferred to the custodian. The depositary bank will only issue ADSs in whole numbers.

When a Holder makes a deposit of ordinary shares, a Holder will be responsible for transferring good and valid title to the depositary bank. As such, a Holder will be deemed to represent and warrant that:

- The ordinary shares are duly authorized, validly issued, fully paid, non-assessable and legally obtained.
- All preemptive (and similar) rights, if any, with respect to such ordinary shares have been validly waived or exercised.
- A Holder is duly authorized to deposit the ordinary shares.
- The ordinary shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, and are not, and the ADSs issuable upon such deposit will not be, "restricted securities" (as defined in the deposit agreement).
- The ordinary shares presented for deposit have not been stripped of any rights or entitlements.

If any of the representations or warranties are incorrect in any way, we and the depositary bank may, at a Holder's cost and expense, take any and all actions necessary to correct the consequences of the misrepresentations.

Transfer, Combination and Split Up of ADRs

ADR Holders will be entitled to transfer, combine or split up such Holder's ADRs and the ADSs evidenced thereby. For transfers of ADRs, a Holder will have to surrender the ADRs to be transferred to the depositary bank and also must:

- ensure that the surrendered ADR is properly endorsed or otherwise in proper form for transfer;
- provide such proof of identity and genuineness of signatures as the depositary bank deems appropriate;
- provide any transfer stamps required by the State of New York or the United States; and
- pay all applicable fees, charges, expenses, taxes and other government charges payable by ADR holders pursuant to the terms of the deposit agreement, upon the transfer of ADRs.

To have a Holder's ADRs either combined or split up, such Holder must surrender the ADRs in question to the depositary bank with such Holder's request to have them combined or split up, and such Holder must pay all applicable fees, charges and expenses payable by ADR holders, pursuant to the terms of the deposit agreement, upon a combination or split up of ADRs.

Withdrawal of Ordinary Shares Upon Cancellation of ADSs

ADS Holders will be entitled to present such Holder's ADSs to the depositary bank for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. A Holder's ability to withdraw the ordinary shares held in respect of the ADSs may be limited by U.S. and English considerations applicable at the time of withdrawal. In order to withdraw the ordinary shares represented by a Holder's ADSs, such Holder will be required to pay to the depositary bank the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares being withdrawn. A Holder assumes the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

The depositary bank may ask a Holder to provide proof of identity and genuineness of any signature and such other documents as the depositary bank may deem appropriate before it will cancel a Holder's ADSs. The withdrawal of the ordinary shares represented by a Holder's ADSs may be delayed until the depositary bank receives satisfactory evidence of compliance with all applicable laws and regulations. Please keep in mind that the depositary bank will only accept ADSs for cancellation that represent a whole number of securities on deposit.

Holders will have the right to withdraw the securities represented by such Holder's ADSs at any time except for:

- Temporary delays that may arise because (i) the transfer books for the ordinary shares or ADSs are closed, or (ii) ordinary shares are immobilized on account of a shareholders' meeting or a payment of dividends;
- Obligations to pay fees, taxes and similar charges; and
- Restrictions imposed because of laws or regulations applicable to ADSs or the withdrawal of securities on deposit.

The deposit agreement may not be modified to impair a Holder's right to withdraw the securities represented by a Holder's ADSs except to comply with mandatory provisions of law.

Voting Rights

Holders generally have the right under the deposit agreement to instruct the depositary bank to exercise the voting rights for the ordinary shares represented by a Holder's ADSs. The voting rights of holders of ordinary shares are described above in "Ordinary Shares—Voting Rights."

At our request, the depositary bank will distribute to a Holder any notices of shareholders' meetings received from us together with information explaining how to instruct the depositary bank to exercise the voting rights of the securities represented by ADSs.

If the depositary bank timely receives voting instructions from a holder of ADSs, it will endeavor to vote the securities (in person or by proxy) represented by the holder's ADSs in accordance with the voting instructions received from such holder and as follows.

- In the event of voting by show of hands, the Depositary will vote (or cause the custodian to vote) all Shares held on deposit at that time in accordance with the voting instructions received from a majority of holders of ADSs who provide timely voting instructions.
- In the event of voting by poll, the Depositary will vote (or cause the custodian to vote) the Shares held on deposit in accordance with the voting instructions received from the holders of ADSs. Under certain limited circumstances described in the deposit agreement, a person designated by us shall be entitled to vote the Shares held on deposit for which voting instructions have not been timely received by the depositary from holders of ADSs.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated herein). Please note that the ability of the depositary bank to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities on deposit. We cannot assure that Holders will receive voting materials in time to enable such Holder to return voting instructions to the depositary bank in a timely manner.

Fees and Charges

The following table shows the fees and charges that a holder of our ADSs may have to pay, either directly or indirectly. These fees and charges are set by the Depositary and are subject to change:

Service	Fees
Issuance of ADSs	Up to U.S. 5¢ per ADS issued
Cancellation of ADSs	Up to U.S. 5¢ per ADS canceled
Distribution of cash dividends or other cash distributions	Up to U.S. 5¢ per ADS held
Distribution of ADSs pursuant to stock dividends, free stock distributions or exercise of rights	Up to U.S. 5¢ per ADS held
Distribution of securities other than ADSs or rights to purchase additional ADSs	Up to U.S. 5¢ per ADS held
Depositary Services	Up to U.S. 5¢ per ADS held on the applicable record date(s) established by the depositary bank

As an ADS holder you will also be responsible for paying certain fees and expenses incurred by the depositary bank and certain taxes and governmental charges such as:

- Fees for the transfer and registration of Shares or other deposited securities, including those charged by the registrar and transfer agent for the Shares in England and Wales (i.e., upon deposit and withdrawal of Shares).
- Expenses incurred for converting foreign currency into U.S. dollars.
- Expenses for cable, telex and fax transmissions and for delivery of securities.
- Taxes and duties (including applicable interest and penalties) and other governmental charges, including upon the transfer of securities (i.e., when Shares are deposited or withdrawn from deposit).

- Fees and expenses as are incurred by the depositary bank in connection with compliance with exchange control regulations and other regulatory requirements applicable to Shares, deposited securities, ADSs and ADRs.
- Fees and expenses incurred in connection with the delivery or servicing of Shares and other property on deposit.

Depositary fees payable upon the issuance and cancellation of ADSs are typically paid to the depositary bank by the brokers (on behalf of their clients) receiving the newly issued ADSs from the depositary bank and by the brokers (on behalf of their clients) delivering the ADSs to the depositary bank for cancellation. The brokers in turn charge these fees to their clients. Depositary fees payable in connection with distributions of cash or securities to ADS holders and the depositary services fee are charged by the depositary bank to the holders of record of ADSs as of the applicable ADS record date.

The Depositary fees payable for cash distributions are generally deducted from the cash being distributed. In the case of distributions other than cash (i.e., stock dividend, rights), the depositary bank charges the applicable fee to the ADS record date holders concurrent with the distribution. In the case of ADSs registered in the name of the investor (whether certificated or uncertificated in direct registration), the depositary bank sends invoices to the applicable record date ADS holders. In the case of ADSs held in brokerage and custodian accounts (via DTC), the depositary bank generally collects its fees through the systems provided by DTC (whose nominee is the registered holder of the ADSs held in DTC) from the brokers and custodians holding ADSs in their DTC accounts. The brokers and custodians who hold their clients' ADSs in DTC accounts in turn charge their clients' accounts the amount of the fees paid to the depositary banks.

In the event of a refusal to pay the depositary fees, the depositary bank may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary fees from any distribution to be made to the ADS holder.

Note that the fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary bank. You will receive prior notice of such changes.

The depositary bank may reimburse us for certain expenses incurred by us in respect of the ADS program established pursuant to the deposit agreement, by making available a portion of the depositary fees charged in respect of the ADS program or otherwise, upon such terms and conditions as we and the depositary bank may agree from time to time.

Amendments and Termination

We may agree with the depositary bank to modify the deposit agreement at any time without a Holder's consent. We undertake to give holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to a Holder's substantial rights any modifications or supplements that are reasonably necessary for the ADSs to be registered under the Securities Act or to be eligible for book-entry settlement, in each case without imposing or increasing the fees and charges such Holder is required to pay. In addition, we may not be able to provide Holders with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

Holders will be bound by the modifications to the deposit agreement if such Holder's continue to hold ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent a Holder from withdrawing the ordinary shares represented by such Holder's ADSs (except as permitted by law).

We have the right to direct the depositary bank to terminate the deposit agreement. Similarly, the depositary bank may in certain circumstances on its own initiative terminate the deposit agreement. In either case, the depositary bank must give notice to the holders at least 30 days before termination. Until termination, a Holder's rights under the deposit agreement will be unaffected.

After termination, the depositary bank will continue to collect distributions received (but will not distribute any such property until a Holder request the cancellation of such Holder's ADSs) and may sell the securities held on deposit. After the sale, the depositary bank will hold the proceeds from such sale and any other funds then held for the holders of ADSs in a non-interest bearing account. At that point, the depositary bank will have no further obligations to holders other than to account for the funds then held for the holders of ADSs still outstanding (after deduction of applicable fees, taxes and expenses).

Books of Depositary

The depositary bank will maintain ADS holder records at its depositary office. Holders may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

The depositary bank will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up and transfer of ADSs. These facilities may be closed from time to time, to the extent not prohibited by law.

Limitations on Obligations and Liabilities

The deposit agreement limits our obligations and the depositary bank's obligations to Holders. Please note the following:

- We and the depositary bank are obligated only to take the actions specifically stated in the deposit agreement without negligence or bad faith.
- The depositary bank disclaims any liability for any failure to carry out voting instructions, for any manner in which a vote is cast or for the effect of any vote, provided it acts in good faith and in accordance with the terms of the deposit agreement.
- The depositary bank disclaims any liability for any failure to determine the lawfulness or practicality of any action, for the content of any document forwarded to Holders on our behalf or for the accuracy of any translation of such a document, for the investment risks associated with investing in ordinary shares, for the validity or worth of the ordinary shares, for any tax consequences that result from the ownership of ADSs, for the credit-worthiness of any third party, for allowing any rights to lapse under the terms of the deposit agreement, for the timeliness of any of our notices or for our failure to give notice.
- We and the depositary bank will not be obligated to perform any act that is inconsistent with the terms of the deposit agreement.
- We and the depositary bank disclaim any liability if we or the depositary bank are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or future of any law or regulation, or by reason of present or future provision of any provision of our articles of association or any provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our control.
- We and the depositary bank disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our articles of association or in any provisions of or governing the securities on deposit.
- We and the depositary bank further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting Shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information.
- We and the depositary bank also disclaim liability for the inability by a holder to benefit from any distribution, offering, right or other benefit that is made available to holders of ordinary shares but is not, under the terms of the deposit agreement, made available to Holders.
- We and the depositary bank may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.
- We and the depositary bank also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.
- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.

Taxes

A Holder will be responsible for the taxes and other governmental charges payable on the ADSs and the securities represented by the ADSs. We, the depositary bank and the custodian may deduct from any distribution the taxes and governmental charges payable by holders and may sell any and all property on deposit to pay the taxes and governmental charges payable by holders. You will be liable for any deficiency if the sale proceeds do not cover the taxes that are due.

The depositary bank may refuse to issue ADSs, to deliver, transfer, split-up or combine ADRs or to release securities on deposit until all taxes and charges are paid by the applicable holder. The depositary bank and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depositary bank and to the custodian proof of taxpayer status and residence and such other information as the depositary bank and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depositary bank and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign Currency Conversion

The depositary bank will arrange for the conversion of all foreign currency received into U.S. dollars if such conversion is practical, and it will distribute the U.S. dollars in accordance with the terms of the deposit agreement. You may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

If the conversion of foreign currency is not practicable or lawful, or if any required approvals are denied or not obtainable at a reasonable cost or within a reasonable period, the depositary bank may take the following actions in its discretion:

- Convert the foreign currency to the extent practical and lawful and distribute the U.S. dollars to the holders for whom the conversion and distribution is lawful and practical.
- Distribute the foreign currency to holders for whom the distribution is lawful and practical.
- Hold the foreign currency (without liability for interest) for the applicable holders.

Governing Law/Waiver of Jury Trial

The deposit agreement, the ADRs and the ADSs will be interpreted in accordance with the laws of the State of New York. The rights of holders of ordinary shares (including ordinary shares represented by ADSs) are governed by the laws of England and Wales.

As an owner of ADSs, holders irrevocably agree that any legal action arising out of the Deposit Agreement, the ADSs or the ADRs, involving the Company or the Depositary, may only be instituted in a state or federal court in the city of New York.

Exhibit 21.1

Subsidiaries of Registrant

Name of undertaking	**Country of registration**
GW Pharma Limited	England and Wales
GW Research Limited	England and Wales
Greenwich Biosciences, Inc.	United States
GWP Trustee Company Limited	England and Wales
GW Pharmaceuticals Australia Pty. Limited	Australia
GW UK Services Limited	England and Wales
GW Global Services (International) Limited	England and Wales
G-Pharm Limited	England and Wales
GW Pharma (Germany) GmbH	Germany
GW Pharma (Italy) S.R.L.	Italy
GW Pharma (Spain) S.A.	Spain
GW Pharma (France) SARL	France
GW Pharma (International) B.V.	Netherlands

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-229308 on Form S-3 and Registration Statement Nos. 33-217328 and 333-204389 on Form S-8 of our report dated November 28, 2018, relating to the financial statements of GW Pharmaceuticals plc appearing in this Annual Report on Form 10-K for the year ended December 31, 2019.

/s/ DELOITTE LLP

London, United Kingdom
February 27, 2020

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-217328 and 333-204389 on Form S-8 and Registration Statement No. 333-229308 on Form S-3 of our report dated February 27, 2020, relating to the financial statements of GW Pharmaceuticals plc and its subsidiaries (the "Company") and the effectiveness of the Company's internal control over financial reporting appearing in this Annual Report on Form 10-K for the year ended December 31, 2019.

/s/ DELOITTE & TOUCHE LLP

San Diego, California
February 27, 2020

EXHIBIT 31.1

Certification of Principal Executive Officer
Pursuant to Exchange Act Rule 13a-14(a)/15d-14(a) as Adopted Pursuant to
Section 302 of the Sarbanes-Oxley Act of 2002

I, Justin Gover, certify that:

1. I have reviewed this Annual Report on Form 10-K of GW Pharmaceuticals plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)), for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected or is reasonably likely to materially affect the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2020

/s/ Justin Gover
Justin Gover
Chief Executive Officer and Director
(Principal Executive Officer)

EXHIBIT 31.2

Certification of Principal Financial Officer
Pursuant to Exchange Act Rule 13a-14(a)/15d-14(a) as Adopted Pursuant to
Section 302 of the Sarbanes-Oxley Act of 2002

I, Scott Giacobello, certify that:

1. I have reviewed this Annual Report on Form 10-K of GW Pharmaceuticals plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)), for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected or is reasonably likely to materially affect the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2020

/s/ Scott Giacobello
Scott Giacobello
Chief Financial Officer
(Principal Financial and Accounting Officer)

EXHIBIT 32.1

Certification
Pursuant to 18 U.S.C. Section 1350 As Adopted Pursuant to
Section 906 of the Sarbanes-Oxley Act of 2002

Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, each of the undersigned hereby certifies, that, to his knowledge:

1. The Annual Report on Form 10-K for the year ended December 31, 2019 (the "Report") of the Company fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 27, 2020

/s/ Justin Gover
Justin Gover
Chief Executive Officer and Director
(Principal Executive Officer)

Date: February 27, 2020

/s/ Scott Giacobello
Scott Giacobello
Chief Financial Officer
(Principal Financial and Accounting Officer)

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. Section 1350, and is not being filed for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference to any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.