CUMBERLAND PHARMACEUTICALS INC
Form 10-K
March 12, 2019
0001087294Non-accelerated
Filer12/31/20182018FYFALSEFALSEFALSEFALSENoNoYes--12-31——100,000,000100,000,00015,723,07516,074,17615
remaining lease term315450,00050,00000010872942018-01-012018-12-31iso4217:USD00010872942018-06-29xbrli:shares00

UNITED STATES SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

Form 10-K

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

For the fiscal year ended December 31, 2018

of

CUMBERLAND PHARMACEUTICALS INC.

A Tennessee Corporation
IRS Employer Identification No. 62-1765329
Commission file number 001-33637

2525 West End Avenue, Suite 950
Nashville, Tennessee 37203
(615) 255-0068

Cumberland Pharmaceuticals Inc. Common Stock, no par value, shares are registered pursuant to Section 12(b) of the Act and are listed on the Nasdaq Global Select Market.

Cumberland Pharmaceuticals Inc. is not a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Cumberland Pharmaceuticals Inc. is required to file reports pursuant to Section 13 or Section 15(d) of the Act. Cumberland Pharmaceuticals Inc. (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, and (2) has been subject to such filing requirements for the past 90 days.

Cumberland Pharmaceuticals Inc. has submitted electronically and posted on its corporate Web site every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months.

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

Cumberland Pharmaceuticals Inc. is a non-accelerated filer as defined in Rule 12b-2 of the Exchange Act and is not a shell company.

The aggregate market value of common stock held by non-affiliates as of June 29, 2018 was $58,282,085. The number of shares of the registrant's Common Stock, no par value, outstanding as of March 5, 2019 was 15,447,413.

DOCUMENTS INCORPORATED BY REFERENCE
Certain information required in Part III of Form 10-K is incorporated by reference from the registrant's Proxy Statement for its 2019 annual meeting of shareholders.

CUMBERLAND PHARMACEUTICALS INC. AND SUBSIDIARIES
Index

PART I

Item 1. Business.

THE COMPANY

Cumberland Pharmaceuticals Inc. ("Cumberland," the "Company," or as used in the context of "we," "us," or "our"), is a specialty pharmaceutical company focused on the acquisition, development and commercialization of branded prescription products. Our primary target markets are hospital acute care, gastroenterology, and oncology supportive care. These medical specialties are characterized by relatively concentrated prescriber bases that we believe can be penetrated effectively by small, targeted sales forces. Cumberland is dedicated to providing innovative products that improve the quality of care for patients and address unmet or poorly met medical needs. We promote our approved products through our hospital and field sales forces in the United States and are establishing a network of international partners to bring our medicines to patients in their countries.

Our portfolio of FDA approved brands includes:

•**Acetadote®** (*acetylcysteine*) Injection, for the treatment of acetaminophen poisoning;

•**Caldolor®** (*ibuprofen*) Injection, for the treatment of pain and fever;

•**Kristalose®** (*lactulose*) for Oral Solution, a prescription laxative, for the treatment of chronic and acute constipation;

•**Omeclamox®-Pak**, (*omeprazole, clarithromycin, amoxicillin*) for the treatment of Helicobacter pylori (*H. pylori*) infection and related duodenal ulcer disease;

•**Vaprisol®** (*conivaptan*) Injection, to raise serum sodium levels in hospitalized patients with euvolemic and hypervolemic hyponatremia;

•**Ethyol®** *(amifostine)* Injection, for the reduction of xerostomia (dry mouth) in patients undergoing post-operative radiation treatment for head and neck cancer and the renal toxicity associated with the administration of cisplatin in patients with advanced ovarian cancer;

•**Totect®** *(dexrazoxane hydrochloride)* Injection, for emergency oncology intervention, to treat the toxic effects of anthracycline chemotherapy in case of extravasation (drug leakage from the bloodstream into the tissues); and

•**Vibativ®** (*telavancin*) Injection, for the treatment of certain serious bacterial infections including hospital-acquired and ventilator-associated bacterial pneumonia, as well as complicated skin and skin structure infections.

Our pipeline of product candidates includes:

•**Hepatoren®** (*ifetroban*) Injection, a Phase II candidate for the treatment of critically ill patients suffering from liver and kidney failure associated with hepatorenal syndrome ("HRS");

•**Boxaban®** *(ifetroban)* Oral Capsules, a Phase II candidate for the treatment of asthma patients with aspirin-exacerbated respiratory disease ("AERD");

•**Vasculan®** *(ifetroban)* Oral Capsules, a Phase II candidate for the treatment of patients with the systemic sclerosis ("SSc") form of autoimmune disease;

•**Portaban®** *(ifetroban)* Injection and Oral Capsules, a Phase II candidate for the treatment of patients with portal hypertension associated with liver disease; and

•**RediTrex™** (*methotrexate*) Injection, an approval submission candidate for the treatment of active rheumatoid, juvenile idiopathic and severe psoriatic arthritis, as well as severe disabling psoriasis.

We have both product development and commercial capabilities and believe we can leverage our existing infrastructure to support our expected growth. Our management team consists of pharmaceutical industry veterans experienced in business development, product development, regulatory, manufacturing, sales marketing and finance. Our business development team identifies, evaluates and negotiates product acquisition, licensing and co-promotion opportunities. Our product development team creates proprietary product formulations, manages our clinical studies, prepares all regulatory submissions and manages our medical call center. Our quality and manufacturing professionals oversee the manufacture, release and shipment of our products. Our marketing and sales professionals are responsible for our commercial activities, and we work closely with our distribution partners to ensure availability and delivery of our products.

Cumberland's growth strategy involves maximizing the potential of our existing brands, while continuing to build a portfolio of differentiated products. We currently market eight FDA approved products for sale in the United States. Through our international partners, we are working to bring our products to patients in their countries. We also look for opportunities to expand our products into additional patient populations through clinical trials, through new indications, and through the support of select investigator-initiated studies. We actively pursue opportunities to acquire additional marketed products, as well as late-stage development product candidates in our target medical specialties. Our clinical team is developing a pipeline of new product candidates to address unmet medical needs. Furthermore, we are supplementing these activities with the earlier stage drug development activities at Cumberland Emerging Technologies ("CET"), our majority-owned subsidiary. CET partners with universities and other research organizations to identify and progress promising, new product candidates, which Cumberland has the opportunity to further develop and commercialize.

We were incorporated in 1999 and have been headquartered in Nashville, Tennessee since inception. During 2009, we completed an initial public offering of our common shares and listing on the Nasdaq stock exchange. Our website address is *www.cumberlandpharma.com*. We make available through our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all material press releases, other filings and amendments to those reports as soon as reasonably practicable after their filing with the U.S. Securities and Exchange Commission, (“SEC”). These filings are also available to the public at *www.sec.gov.*

PRODUCTS

Our key products include:

Products	Indication	Status
Acetadote®	Acetaminophen Poisoning	Marketed
Caldolor®	Pain and Fever	Marketed
Kristalose®	Chronic and Acute Constipation	Marketed
Omeclamox®-Pak	H. pylori infection and related Duodenal Ulcer disease	Marketed
Vaprisol®	Euvolemic and Hypervolemic Hyponatremia	Marketed
Ethyol®	Radiation xerostomia and chemotherapy renal toxicity	Marketed
Totect®	Toxic chemotherapy extravasation	Marketed
Vibativ®	Serious bacterial infections	Marketed
Hepatoren®	Hepatorenal Syndrome	Phase II
Boxaban®	Aspirin-Exacerbated Respiratory Disease	Phase II
Vasculan®	Systemic Sclerosis	Phase II
Portaban®	Portal Hypertension associated with liver disease	Phase II
RediTrex™	Arthritis and psoriasis	Pre-approval

Acetadote®

Acetadote is an intravenous formulation of N-acetylcysteine, indicated for the treatment of the liver toxicity associated with acetaminophen poisoning. Acetadote, has been available in the United States since Cumberland's 2004 introduction of the product through our hospital sales force. Acetadote is typically used in hospital emergency departments to prevent or lessen potential liver damage resulting from an overdose of acetaminophen, a common ingredient in many over-the-counter and prescription pain relieving and fever-reducing products. Acetaminophen continues to be a leading cause of poisonings reported by hospital emergency departments in the United States, and Acetadote has become a standard of care for treating this potentially life-threatening condition.

Acetadote received U.S. Food and Drug Administration ("FDA") approval as an orphan drug, which provided seven years of marketing exclusivity from the date of approval. In connection with the FDA's approval of Acetadote, we committed to certain post-marketing activities for the product. Completion of our first Phase IV commitment resulted in the FDA's 2006 approval of expanded labeling for the product for use in pediatric patients. Completion of our second Phase IV commitment resulted in further revised labeling for the product with FDA approval of additional safety data in 2008. Completion of our third and final Phase IV commitment in 2010 culminated in the FDA’s approval of a new formulation for the product. The next generation formulation, contains no ethylene diamine tetracetic acid

("EDTA") or other stabilization agent, chelating agent or preservative. In early 2011, Cumberland introduced this new Acetadote formulation replacing the original form of the product which we no longer manufacture.

In June 2013, the FDA approved updated labeling for Acetadote revising the product's indication and providing new dosing guidance for specific patient populations. As a result, dosing guidance is now included for patients weighing over 100 kg, and new language has been added to alert health care providers that, in certain clinical situations, therapy should be extended for some patients.

Beginning in 2012, the United States Patent and Trademark Office (the "USPTO") issued us a series of patents associated with our Acetadote product. These patents are discussed in Part I, Item I, "*Business - Trademarks and Patents*" of this Form 10-K. On November 8, 2012, we learned that the FDA approved an abbreviated new drug application (ANDA) filed by InnoPharma, Inc. and referencing Acetadote. That product, with the old formulation containing EDTA, was subsequently introduced by APP, a division of Fresenius Kabi USA, at the end of 2012. In early 2013, we entered into an agreement with Perrigo Company resulting in the distribution of our Authorized Generic acetylcysteine injection (our "Authorized Generic") product. Both Acetadote and our Authorized Generic utilize the new, EDTA-free formulation which accounted for continued significant market share during 2018.

In November 2015, an Illinois judge issued a final ruling in favor of Cumberland Pharmaceuticals Inc. in a patent case associated with Acetadote. By ruling in Cumberland's favor, the court upheld the validity of the patent which encompasses our EDTA-Free formulation and has a term until August 2025. The court also granted a permanent injunction preventing challengers from marketing a generic version of our proprietary Acetadote product formulation before the expiration of Cumberland’s patent in August 2025.

On January 26, 2017, an Appeals Court affirmed the District Court ruling in the Company's favor upholding Cumberland's Acetadote patent and expressly rejected the validity challenge.

Caldolor®

Caldolor, our intravenous formulation of ibuprofen, was the first injectable product approved in the U.S. for the treatment of both pain and fever. We conducted a series of clinical studies in over nine hundred adult patients to develop the data to support our FDA submission for the product's registration. The FDA approved Caldolor for marketing in the United States in 2009 following a priority review. The product was indicated for use by adults for the management of mild to moderate pain and the management of moderate to severe pain as an adjunct to opioid analgesics. It was also the first FDA approved intravenous therapy for treating fever.

In late 2009, we launched Caldolor and stocked the product at major wholesalers serving hospitals nationwide. We initially worked to establish a core group of medical facilities approving and purchasing the product and then focused on building more sales volume and treating a broader range of patients within those stocked facilities. We promote Caldolor in the United States through our dedicated hospital sales force.

We completed a series of Phase IV studies to gather additional data to support our Caldolor product. Those clinical trials involved another 1,000 patients, adult and pediatric patients. These studies included data on a shortened infusion time and pre-surgical administration of the product. To address our Phase IV commitment to the FDA, these studies also included evaluation of the product for the reduction of fever in hospitalized children and the treatment of pain in children undergoing tonsillectomy surgeries.

In 2015 we received FDA approval for the use of Caldolor in pediatric patients six months of age and older. Caldolor is the first and only injectable non-steroidal anti-inflammatory drug (NSAID) approved for use in children. We then initiated a study to collect data on the use of Caldolor in children ranging in age from birth up to six months of age. Enrollment in that study progressed in 2018.

In early 2018, we completed and filed the application for FDA approval of a next generation Caldolor product featuring an improved package and formulation. In April 2018, the FDA determined that the application was complete and notified us of their acceptance of the submission for review. There were then a number of communications with questions addressed through multiple amendments that were submitted to the application. On August 2, 2018, we received a complete response from the FDA outlining the additional information needed for the application’s approval. We held a teleconference with the FDA to discuss their additional requirements. In September 2018, the Company submitted an amendment to our application containing additional quality and nonclinical data. As noted in the "Subsequent Events" section of this Item, the application was subsequently approved by the FDA.

Kristalose®

Kristalose is a prescription laxative administered orally for the treatment of acute and chronic constipation. An innovative, dry powder crystalline formulation of lactulose, Kristalose is designed to enhance patient acceptance and compliance. Kristalose is the only prescription laxative available in pre-measured powder packets. Kristalose dissolves easily in four ounces of water, offering patients a virtually taste-free, grit-free and essentially calorie-free alternative to lactulose syrups. We conducted a preference study which indicated that seventy-seven percent of patients surveyed prefer the taste, consistency and portability of Kristalose over similar products in syrup forms.

We acquired exclusive U.S. commercialization rights to Kristalose in 2006, assembled a dedicated field sales force and re-launched it in September 2006 as a Cumberland brand. We direct our sales efforts to physicians who are the most prolific writers of prescription laxatives, including gastroenterologists and internists. We supplement this personal promotion with telemarketing campaigns to expand our reach and support of the product.

In late 2011, through a series of transactions, we entered into an agreement with Mylan Inc. to acquire certain assets associated with the Kristalose brand including the Kristalose trademark and the FDA registration.

Using the preference data as a cornerstone of our marketing efforts, we repositioned the brand in early 2014. The marketing strategy which continued in 2018 included an enhanced patient coupon program and expanded managed care coverage for the product.

We added a co-promotion partner to provide support for the brand in 2017. Poly Pharmaceuticals is promoting Kristalose to physician targets not covered by our field sales forces. In 2018 we added another co-promotion partner, 2R Pharmaceuticals who is repackaging Kristalose and featuring it with additional new physician targets.

Omeclamox®-Pak

Many ulcers of the gastrointestinal tract are caused by an infection from the Helicobacter pylori (“H. pylori”) bacterium. Omeclamox-Pak is a branded prescription product used for the treatment of these infections and the related duodenal ulcer disease. This innovative product combines three well-known and widely prescribed medications: omeprazole, clarithromycin, and amoxicillin. Omeclamox-Pak was the first FDA approved triple therapy combination medication to contain omeprazole as the proton pump inhibitor, which works to decrease the amount of acid the stomach produces. Clarithromycin and amoxicillin are both antibiotic agents which hinder the growth of the H. pylori bacteria. Interaction of these agents allows the stomach lining to heal effectively. The medications are packaged together on convenient daily dosing cards, making it simple to follow the twice a day dosing before meals.

While there are competing combination products, Omeclamox-Pak is one of the few actively marketed brands for this condition. In addition, compared to the competitors, Omeclamox-Pak involves the lowest pill burden and fewest days of therapy. Our involvement with Omeclamox-Pak began in October 2013, through a co-promotion agreement with Pernix Therapeutics ("Pernix"). In November 2015, Cumberland entered into an exclusive license and supply agreement with Gastro-Entero Logic, LLC (“GEL”), assumed full commercial responsibility for Omeclamox-Pak in the United States, and concluded our agreements with Pernix. Cumberland became responsible for the distribution, national accounts and all sales promotion of Omeclamox-Pak under the GEL agreement.

In December 2018, we closed on an agreement with GEL to acquire all remaining assets associated with Omeclamox-Pak including the Product’s FDA-approved New Drug Application, the domestic and international trademarks. The closing of this transaction ended Cumberland’s payments of royalties and manufacturing fees to GEL, and we assumed responsibility for the maintenance of the Product’s FDA approval and for the oversight of the Product’s manufacturing and packaging.

Our field sales force promotes Omeclamox-Pak to the gastroenterology market segment, which accounts for the largest component of the prescriber base for this product. We supplement this personal promotion through telemarketing campaigns to expand the support and use of the product. We have also established a series of contracts to provide managed care coverage for Omeclamox-Pak.

Vaprisol®

In early 2014, we entered into an agreement with Astellas Pharma US, Inc. ("Astellas") to acquire Vaprisol, including certain product rights, intellectual property and related assets. Vaprisol is a prescription brand indicated to raise serum sodium levels in hospitalized patients with euvolemic and hypervolemic hyponatremia. The product was developed and registered by Astellas and then launched in 2006. It is one of two branded prescription products indicated for the treatment of hyponatremia, and the only intravenously administered branded treatment.

Hyponatremia, an imbalance of serum sodium to body water, is the most common electrolyte disorder among hospitalized patients. These electrolyte disturbances occur when the sodium ion concentration in the plasma is lower than normal and are often associated with a variety of critical care conditions including congestive heart failure, liver failure, kidney failure and pneumonia. Vaprisol raises serum sodium to appropriate levels and promotes free water secretion.

We re-launched active promotion of the brand during the middle of 2014 utilizing our hospital sales force supported by a series of marketing initiatives. In late 2017, we encountered delays in manufacture and supply of the product which impacted its sales until the second quarter of 2018 when new inventory arrived. We then restocked the distribution channels for Vaprisol and increased our inventory level of the brand.

Ethyol®

In May 2016, the Company announced an agreement with Clinigen Group Plc ("Clinigen") in which Cumberland acquired the exclusive rights to commercialize Ethyol in the United States. Ethyol is an FDA approved cytoprotective drug containing amifostine for injection. It is indicated as an adjuvant therapy to reduce the incidence of xerostomia (dry mouth) as a side-effect in patients undergoing post-operative radiation treatment for head and neck cancer. It also reduces the cumulative renal toxicity associated with the repeated administration of cisplatin in patients with advanced ovarian cancer. Under the terms of the agreement, Cumberland is responsible for all marketing, promotion, and distribution of the product in the United States.

In late 2016, we began distribution of Ethyol for injection to wholesalers within the United States and launched national promotional support for the brand by our hospital sales division.

In early 2018, we announced a publication in *Leukemia and Lymphoma*, with study results showing that amifostine decreases gastro-intestinal toxicity in patients who receive treatment for their multiple myeloma. In September 2018 the Company announced a publication in *Lung Cancer: Targets and Therapy* of a contemporary retrospective study showing that subcutaneous amifostine administered before radiotherapy postponed the onset of acute esophagitis in stage three small cell lung cancer patients treated with concomitant doublet chemotherapy and hyperfractionated radiotherapy.

Totect®

In January 2017, we announced an exclusive agreement with Clinigen to commercialize the oncology support drug, Totect in the United States. It is an FDA approved hospital based emergency oncology intervention drug, indicated to treat the toxic effects of anthracycline chemotherapy. It treats anthracycline extravasation that occurs when the injected medication escapes from the blood vessels and circulates into surrounding tissues in the body, causing severe damage and serious complications. Totect can limit such damage without the need for additional surgeries or procedures and enables patients to continue their essential anti-cancer treatment.

In late July 2017, we initiated distribution and sale of Totect (dexrazoxane hydrochloride) in the United States. This followed the FDA approval of the updated labeling and product manufacturer for the product. In late September 2017, we announced the launch of Totect promotion in the United States.

We launched Totect during a national shortage of dexrazoxane in late 2017, resulting in strong initial demand for the product. During 2018 a number of competitive products returned, reducing Totect’s share of the market.

Vibativ®

In November 2018, the Company announced an agreement with Theravance Biopharma ("Theravance") to acquire the Vibativ assets from Theravance and assume global responsibility for Vibativ including the marketing, distribution, manufacturing and regulatory activities associated with the brand. Vibativ is a patented, FDA approved injectable anti-infective for the treatment of certain serious bacterial infections including hospital-acquired and ventilator-associated bacterial pneumonia and complicated skin and skin structure infections. It addresses a range of Gram-positive bacterial pathogens, including those that are considered difficult-to-treat and multidrug-resistant. Immediately after the closing, we initiated shipments of Vibativ and assumed responsibility for the supply chain and distribution of the product in the U.S. Vibativ is supported by our hospital sales division.

Hepatoren®

In 2011, we entered into an agreement to acquire the rights to ifetroban, a new Phase II product candidate. Our acquisition of the rights to the ifetroban program includes an extensive clinical database and non-clinical data package as well as manufacturing processes, know-how and intellectual property. Ifetroban was initially developed by a large pharmaceutical company for significant cardiovascular indications. That company conducted extensive studies for their target indications and eventually donated the entire program to Vanderbilt University. Researchers at Vanderbilt identified ifetroban as a potentially valuable compound in treating patients for several niche indications. Cumberland acquired the rights to the ifetroban program from Vanderbilt through CET with the intention to develop the product for several potential new indications.

We have commenced manufacturing of an intravenous formulation of ifetroban and the FDA has cleared our IND application for this product candidate. We have initiated clinical development under the brand name Hepatoren and are evaluating this candidate for the treatment of critically ill hospitalized patients suffering from hepatorenal syndrome ("HRS"). HRS is a life threatening condition involving liver and kidney failure, with a high mortality rate and no approved pharmaceutical therapy in the U.S. We completed a sixty-four patient Phase II study to evaluate the safety, efficacy and pharmacokinetics of escalating doses of Hepatoren in HRS patients. Progression to higher dose levels was reviewed and approved by an independent safety committee. The study was stratified into Type I or Type II patients with HRS based upon the progression of their disease.

Top line results from this study indicated that Hepatoren was overall well tolerated in the HRS patients with no safety concerns noted. We have filed the results from this study with the FDA and began evaluating the design for a follow-on Phase II efficacy study. During 2018 we decided to await results from our other Phase II ifetroban studies before determining the strategy for the best path to approval for ifetroban, our first new chemical entity.

Boxaban®

We have completed the manufacturing and initiated clinical development of an oral formulation of ifetroban under the brand name Boxaban. We are evaluating this candidate for patients suffering from Aspirin-Exacerbated Respiratory Disease ("AERD"), also known as Samter’s Triad, a chronic medical condition that consists of three clinical features: asthma, sinus disease with nasal polyposis and sensitivity to aspirin. AERD is characterized by sharp increases in inflammatory mediators and platelet activity within the respiratory system. Approximately one in twenty asthmatic adults in the U.S. suffer from AERD and awareness of the disease is growing within the medical community. There is no U.S. approved pharmaceutical treatment for AERD.

We completed an initial Phase II clinical study to evaluate the safety and tolerability of Boxaban in AERD patients. The multicenter study involved sixteen patients at several U.S. medical centers led by the Scripps Research Institute. Results indicated that Boxaban was well tolerated with no safety concerns noted in patients with a history of AERD. In early 2017, the FDA cleared Cumberland’s investigational new drug (“IND”) application for the Company’s AERD clinical program. Following this clearance, we initiated a follow-on multicenter Phase II efficacy study to evaluate the efficacy of Boxaban in seventy-six patients with symptomatic AERD. Enrollment in this multi-center, placebo controlled study progressed in 2018 at a growing number of allergy and asthma centers across the United States.

Vasculan®

In April 2016, we announced the addition of Vasculan to our pipeline. Through Cumberland's ifetroban program, Cumberland has initiated the clinical development of ifetroban oral capsules for the treatment of systemic sclerosis. Systemic sclerosis (SSc), also called scleroderma, is a debilitating autoimmune disorder characterized by diffuse fibrosis of the skin and internal organs, as well as vascular dysfunction. Preclinical studies have shown that ifetroban prevents and can restore cardiac function in a preclinical model of pulmonary arterial hypertension. This disease has a high morbidity and the highest case-specific mortality of any rheumatic disorder with 50% of patients dying or developing major internal organ complications within 3 years of diagnosis.

Although several medications are used to treat the skin disease associated with SSc, there is no universally effective treatment to improve the function of affected internal organs such as the lungs, heart, and gastrointestinal tract.

The FDA has cleared our IND to evaluate the safety and efficacy of Vasculan in patients with SSc. As a result, we initiated a Phase II multicenter study in thirty-four SSc patients. Enrollment in this randomized, placebo controlled trial progressed at several scleroderma centers of excellence in the United States during 2018.

Portaban®

In September 2016, we announced the addition of Portaban to our pipeline. Cumberland has initiated the clinical development of Portaban for the treatment of portal hypertension ("PH") associated with chronic liver disease. Preclinical studies have shown ifetroban can reduce portal pressure, inflammation, and fibrosis in multiple models of liver injury.

The FDA cleared our IND for a clinical development program evaluating Portaban in thirty patients with PH. Following that clearance, a multicenter Phase II study was initiated. During 2018 enrollment in this randomized, placebo controlled study was completed.

This study was primarily designed to evaluate the safety of ifetroban treatment in this population and was not powered for any efficacy measurement. An initial review of the data from the study shows ifetroban was safe and well tolerated with no unexpected safety findings.

We also measured hepatic venous pressure. Patients enrolled had a greater degree of variability than expected in their hepatic venous pressure gradient, therefore no definitive conclusions could be made on the impact of ifetroban on modulating that gradient. A full analysis of the data to include biomarkers and exploratory endpoints is ongoing. We will now await results from our other Phase II ifetroban studies before deciding on the best path for approval for ifetroban, our first new chemical entity.

RediTrex™

In November 2016, we announced that we had entered into an Agreement with Nordic Group B.V. to commercialize their methotrexate product line in the United States which is designed for treating patients with arthritis and psoriasis. Cumberland is responsible for the registration and commercialization of these products while Nordic will handle the product’s supply. Nordic has registered and is selling their methotrexate products in several European countries.

During late 2018, we completed the submission and filed with the FDA a New Drug Application for the approval of our methotrexate product line. This filing follows two meetings held with the FDA to discuss the approval pathway and requirements for the submission. As noted in the "Subsequent Event" section of this Item, the FDA subsequently determined that the application was complete and ready for their review.

OUR STRATEGY

Our growth strategy involves maximizing the potential of our existing brands while continuing to build a portfolio of differentiated products. We currently market eight FDA approved products for sale in the United States. Through our international partners, we are working to bring our products to patients in their countries. We also look for opportunities to expand our products into additional patient populations through clinical trials, new indications, and select investigator-initiated studies. We actively pursue opportunities to acquire additional marketed products as well as late-stage development product candidates in our target medical specialties. Our clinical team is developing a pipeline of new product candidates to address unmet medical needs. Further, we are supplementing these activities with the early stage drug development activities at Cumberland Emerging Technologies ("CET"), our majority-owned subsidiary. Specifically, we are seeking long term sustainable growth by executing the following plans:

Support and expand the use of our marketed products. We continue to evaluate our products following their FDA approval to determine if additional clinical data could expand their market and use. We will continue to explore opportunities for label expansion to bring our products to new patient populations. We have secured pediatric approval, expanding the labeling for both our Acetadote and Caldolor brands.

Selectively add complementary brands. In addition to our product development activities, we are also seeking to acquire products or late-stage development product candidates to continue to build a portfolio of complementary brands. We focus on under-promoted, FDA approved drugs as well as late-stage development products that address poorly met medical needs. We will continue to target product acquisition candidates that are competitively differentiated, have valuable intellectual property or other protective features, and allow us to leverage our existing infrastructure. Our acquisition of Vibativ represents our largest product acquisition.

Progress clinical pipeline and incubate future product opportunities at CET. We believe it is important to build a pipeline of innovative new product opportunities. Our ifetroban Phase II development programs represent the implementation of this strategy. At CET, we are supplementing our acquisition and late-stage development activities with the early-stage drug development activities. CET partners with universities and other research organizations to develop promising, early-stage product candidates, which Cumberland has the opportunity to further develop and commercialize. We expanded our network of University collaborations with the addition of Louisiana State University and the Medical University of South Carolina.

Leverage our infrastructure through co-promotion partnerships. We believe that our commercial infrastructure can help drive prescription volume and product sales. We look for strategic partners that can complement our capabilities and enhance the opportunity for our brands. Our recent co-promotion partnership with Poly Pharmaceuticals, Inc. allows us to expand current promotional support for Kristalose across the United States.

Build an international contribution to our business. We have established our own commercial capabilities, including two sales divisions to cover the U.S. market for our products. We are also building a network of select international partners to register our products and make them available to patients in their countries.

We will continue to develop and expand our network of international partners while supporting our partners' registration and commercialization efforts in their respective territories. The acquisition of Vibativ resulted in several new international partners and market opportunities.

Manage our operations with financial discipline. We continually work to manage our expenses in line with our revenues in order to deliver positive cash flow from operations. We remain in a strong financial position, with favorable gross margins, and a strong balance sheet. We use excess cash flow for our ongoing share repurchase program.

SALES AND MARKETING

Our sales and marketing team has broad industry experience in selling branded pharmaceuticals. Our sales and marketing professionals manage our dedicated hospital and gastroenterology sales forces, including approximately 50 sales representatives and district managers, direct our national marketing campaigns and maintain key national account relationships.

Hospital market: We promote Caldolor, Vaprisol, Acetadote, Ethyol, Totect and Vibativ through our dedicated hospital sales division. This organization targets key hospitals across the U.S. and is comprised of sales professionals with substantial experience in the hospital market. Independent market data continues to indicate that the majority of pharmaceutical promotional spending is directed toward large, outpatient markets on drugs intended for chronic use rather than short-term, hospital use.

We believe the hospital market is under-served and highly concentrated, and that it can be penetrated effectively by a small, dedicated sales force without large-scale promotional activity. Our established position in the hospital market provided the rationale for adding Ethyol and Totect as our first oncology products that complement our hospital product line. Our strategy has been to increase the focus of our hospital sales team on targeted, high priority accounts.

Gastroenterology market: We promote Kristalose and Omeclamox-Pak through a dedicated field sales team addressing a targeted group of physicians who are large prescribers of both products. Because the market for gastrointestinal diseases is broad in patient scope, yet relatively narrow in physician base, we believe it provides product opportunities that can be penetrated with a modest sized sales force.

By investing in our sales and marketing activities we believe that we can increase market share for both products. Our field sales force features both Kristalose and Omeclamox-Pak during most of their physician calls, establishing our presence in the gastroenterology market.

Our marketing executives conduct ongoing analysis to evaluate marketing campaigns and promotional programs. The evaluations include development of product profiles, testing of the profiles against the needs of the market, determining what additional product information or development work is needed to effectively market the products and preparing financial forecasts.

We utilize professional branding and packaging as well as promotional items to support our products, including direct mail, sales brochures, journal advertising, educational and reminder leave-behinds, patient educational pieces, coupons, and product sampling. We also regularly attend select medical meetings and trade shows to expand the awareness of our products.

Our national accounts function is responsible for key large buyers and related marketing programs. National accounts maintains relationships with our wholesaler customers as well as with third-party payors such as group purchasing organizations, pharmacy benefit managers, hospital buying groups, state and federal government purchasers and health insurance companies.

MATERIAL CUSTOMERS

Our primary customers are wholesale pharmaceutical distributors in the United States. Total revenue by customer for each customer representing 10% or more of consolidated gross revenues are summarized below for the year ended December 31, 2018:

	2018
Customer 1	26%
Customer 2	24%
Customer 3	25%
Customer 4	11%

INTERNATIONAL PARTNERSHIPS

We have established our own capabilities to support the commercialization of our products in the U.S. Our international strategy is to identify and partner with other companies that have the appropriate capabilities to support our products in their respective countries. We have entered into a series of agreements to establish an international network, which is summarized in the table below and includes information on our primary partners:

International Partner	Product(s)	Territory	Status
Phebra Pty Ltd	Acetadote	Australia and New Zealand	Marketed
DB Pharm Korea Co., Ltd.	Caldolor	South Korea	Marketed
Seqirus (a CSL company)	Caldolor	Australia and New Zealand	Marketed
Sandor Medicaids Pvt. Ltd.	Caldolor	India, Pakistan, Bangladesh and Nepal	Registration
GerminMED	Caldolor	Qatar and Arabian Peninsula	Registration
PT. ETHICA Industri Farmasi	Caldolor	Indonesia	Registration
Laboratorios Grifols, S.A.	Caldolor	Spain, Portugal and South America	Development
Gloria Pharmaceuticals Co. Ltd.	Caldolor & Acetadote	China and Hong Kong	Development
R-Pharm JSC	Vibativ	Russia	Marketed
Hikma Pharmaceuticals	Vibativ	Arabian Gulf	Registration
MegaPharma Ltd	Vibativ	Isreal and Palestine	Marketed

Our international commercialization agreements include a license to one or more Cumberland products for a specific territory as noted in the table above. We seek partners who have the local infrastructure to support the registration and commercialization of our products in their territory.

Under the terms of our agreements our partners are responsible for:

•Seeking regulatory approvals for the products;
•Launching the brand;
•Managing the ongoing marketing, sales and product distribution;
•Addressing the ongoing regulatory requirements in the international territories;
•Remitting any upfront, regulatory and sales milestone payments;
•Providing the transfer price for supplies of product; and
•Calculating and paying any royalties, as applicable.

Our responsibilities include:

•Providing a dossier of relevant information to support product registration;
•Maintaining our intellectual property associated with the product;
•Sharing our marketing strategy, experience and materials for the brand; and
•Manufacturing and providing finished product for sale.

During 2018 Caldolor was approved for use in India. We also worked to support our existing international partners and to identify new companies to represent our products in select additional territories. During 2018 we reached an understanding with Teligent Pharmaceuticals Inc to end our license for Caldolor in Canada following Teligent's acquisition of our previous partner for that market. Also, during 2018, we began the transition with Theravance for the Vibativ license arrangements for several international markets.

CLINICAL AND REGULATORY AFFAIRS

We have in-house capabilities for the management of our clinical, professional and regulatory affairs. Our team develops and manages our clinical trials, prepares regulatory submissions, manages ongoing product-related regulatory responsibilities and manages our medical information call center. Team members have been responsible for devising the regulatory and clinical strategies for all our products as well as obtaining FDA approvals for Acetadote and Caldolor.

Clinical development

Our clinical development personnel are responsible for:

•creating clinical development strategies;
•designing, implementing and monitoring our clinical trials; and
•creating case report forms and other study-related documents.

Regulatory and quality affairs

Our internal regulatory and quality affairs team is responsible for:

•preparing and submitting INDs for clearance to begin patient studies;
•preparing and submitting NDAs and fulfilling post-approval marketing commitments;
•maintaining investigational and marketing applications through the submission of appropriate reports;
•submitting supplemental applications for additional label indications, product line extensions and manufacturing improvements;
•evaluating regulatory risk profiles for product acquisition candidates, including compliance with manufacturing, labeling, distribution and marketing regulations;
•monitoring applicable third-party service providers for quality and compliance with current Good Manufacturing Practices ("GMPs"), Good Laboratory Practices ("GLPs"), and Good Clinical Practices ("GCPs"), and performing periodic audits of such vendors; and
•maintaining systems for document control, product and process change control, customer complaint handling, product stability studies and annual drug product reviews.

PROFESSIONAL AND MEDICAL AFFAIRS

Our medical team provides in-house, medical information support for our marketed products. This includes interacting directly with healthcare professionals to address any product or medical inquiries through our medical information call center and medical science liaisons. In addition to coordinating the call center, our clinical/regulatory group generates medical information letters, provides informational memos to our sales forces and assists with ongoing training for the sales forces.

CLINICAL DEVELOPMENT AND STUDY RESULTS

Ethyol Study

In January 2018, we announced a new publication in *Leukemia and Lymphoma*, with results from an investigator initiated study showing that amifostine decreases gastro-intestinal (GI) toxicity in patients who receive treatment for their multiple myeloma.

Omeclamox-Pak Study

In March 2018, the Company announced a publication of an open access article in *Infection and Drug Resistance*, with results demonstrating an 85% eradication rate of Helicobacter pylori (H. pylori) infection using clarithromycin-based triple therapy.

New Caldolor Clinical Data

In October 2018, Cumberland announced two favorable Caldolor study publications, adding to the growing library of literature supporting the brand. An investigator initiated study at The Ohio State Wexner Medical Center, published in the journal *Frontiers in Surgery*, revealed more effective pain control and opioid-sparing activity with Caldolor when compared to ketorolac in patients undergoing arthroscopic knee surgery.

Additionally, an investigator initiated trial conducted at Tufts University School of Dental Medicine and published online in the *Journal of Oral and Maxillofacial Surgery*, concluded that preemptive analgesia with Caldolor (IV ibuprofen) is more effective than Ofirmev® (IV acetaminophen) in reducing post-surgical pain and opioid use.

Caldolor Pediatric Study

We previously received FDA approval for the use of Caldolor in pediatric patients six months of age and older. Caldolor is the first and only injectable non-steroidal anti-inflammatory drug (NSAID) approved for use in children. We then initiated a study to collect data on the use of Caldolor in children ranging in age from birth up to six months of age. Enrollment in that multi-center study progressed in 2018.

Ifetroban Phase II Studies

During 2018, we completed study enrollment for Portaban - the Company's Portal Hypertension clinical program. Thirty patients were enrolled in a randomized, double-blind, placebo-controlled pilot study to assess ifetroban for the treatment of portal hypertension in cirrhotic patients. This study was primarily designed to evaluate the safety of ifetroban treatment in this population and was not powered for any efficacy measurement.

An initial review of the data from the study shows ifetroban was safe and well tolerated with no unexpected safety findings. We also measured hepatic venous pressure. Patients enrolled had a greater degree of variability than expected in their hepatic venous pressure gradient, therefore no definitive conclusions could be made on the impact of ifetroban on modulating that gradient. A full analysis of the data to include biomarkers and exploratory endpoints is ongoing. We will now await results from our other Phase II ifetroban studies before deciding on the best path for approval of our first new chemical entity. We also continued to advance our Vasculan and Boxaban clinical pipeline programs, with patient enrollment progressing in each of those Phase II studies

New Hospital Product Candidate Study

Cumberland was responsible for the formulation, development and FDA approval of both Acetadote and Caldolor. Our Medical Advisory Board has helped us identify additional opportunities that address unmet or poorly met medical needs. As a result, Cumberland has successfully designed, formulated and completed the preclinical studies for a cholesterol reducing agent for use in the hospital setting.

During 2017, we completed a Phase I study which defined the pharmacokinetic properties and provided a favorable safety profile for this new product candidate. The study results and a proposed clinical development plan were discussed with the FDA and, as a result, in 2018 a Phase II study was initiated.

BUSINESS DEVELOPMENT

Since inception, we have had an active business development program focused on acquiring rights to marketed products and product candidates that fit our strategy and target markets. We source business development opportunities through our international network of advisory firms and individual pharmaceutical industry and medical advisors. A multi-disciplinary internal management team reviews these opportunities on a regular basis using a list of selection criteria. We have historically focused on product opportunities that are a strategic fit with our commercial organization, development expertise and medical focus, employing a variety of transaction structures. Our additions of Omeclamox-Pak, Vaprisol, Ethyol, Totect and Vibativ reflect our business development process and follow our selection criteria.

We intend to continue to build a portfolio of complementary, niche products largely through product acquisitions and late-stage product development. Our primary targets are under-promoted, FDA approved drugs with existing brand recognition and late-stage development product candidates that address unmet or poorly met medical needs in the hospital acute care and gastroenterology markets. We believe that by focusing mainly on approved or late-stage products, we can minimize the significant risk, cost and time associated with drug development.

Piramal Co-promotion Agreement

In November 2015, we announced a co-promotion agreement with Piramal Critical Care ("Piramal"). Through this agreement, Piramal initiated co-promotion two of Cumberland’s branded hospital products, Caldolor and Vaprisol throughout the United States. Piramal has helped expand Cumberland’s reach for these products by providing coverage to an additional group of hospitals where Piramal’s critical care sales force has existing relationships. The multi-year collaboration provides expanded sales promotion for the two brands, increased communication to medical professionals and enhanced availability of the products to support patient care.

Nordic License Agreement

In November 2016, we announced our agreement to acquire the exclusive U.S. rights to Nordic Group B.V.'s injectable methotrexate product line. The products are designed for the treatment of active rheumatoid arthritis, juvenile idiopathic arthritis, severe psoriatic arthritis, and severe disabling psoriasis. The product line is approved for patient use in various European countries. Cumberland will register and commercialize the methotrexate products in the United States.

Clinigen Strategic Alliance Agreement

We previously entered into a strategic alliance with the Clinigen Group plc ("Clinigen"), an international specialty pharmaceutical and services company, to commercialize select Clinigen products in the U.S. In May 2016, we announced an agreement with Clinigen to acquire an exclusive license and commercialize Ethyol® in the U.S. We then announced in January 2017, our second agreement with Clinigen to acquire an exclusive license and launch Totect® in the U.S.

During August 2017, we entered into a distribution agreement with Clinigen for their Cardioxane® (dexrazoxane hydrochloride, injection) product which is used to support oncology patients from the cardiac complications associated with certain chemotherapeutic agents. Shipments associated with this distribution agreement have been under a special, expedited clearance from the FDA to address the shortage of dexrazoxane in the United States.

Poly Co-Promotion Agreement

In 2017, we entered into a co-promotion arrangement with Poly Pharmaceuticals, Inc. (“Poly”) for our Kristalose product. Poly is a privately held U.S. specialty pharmaceutical company that is featuring Kristalose to an expanded number of physicians. Poly’s sales organization is more than doubling the number of nationwide physicians called upon with Kristalose.

2R and Foxland Agreements

During 2018, we entered into another co-promotion arrangement related to our Kristalose product. We have agreements with 2R Investments, LLC and with Foxland Pharmaceuticals, Inc. to package, distribute and promote an authorized generic form of our Kristalose product to physician targets that we do not cover. Cumberland continues to manage the regulatory activities associated with the product.

CET Collaboration Agreements

Through CET, we collaborate with a select group of academic research institutions located in the mid-south region of the U.S. CET is collaborating with Vanderbilt University, the University of Mississippi, the University of Tennessee Research Foundation, Louisiana State University, and the Medical University of South Carolina to identify, co-develop and seek grant funding for promising biomedical technologies emerging from those research institutions. These arrangements enable CET to team with university-based researchers to advance their scientific discoveries and breakthroughs by designing new product candidates to improve patient care and address unmet medical need.

MANUFACTURING AND DISTRIBUTION

Manufacturing

We partner with third parties for certain non-core, capital-intensive capabilities, including the manufacturing and distribution of our products. We manage these third-party relationships and are responsible for the quality review and release of each lot of our products.

Caldolor®

We have agreements with multiple manufacturers for the supply of Caldolor and during 2018 we obtained commercial supplies from two of these manufacturers for our international and domestic Caldolor requirements.

Acetadote®

For Acetadote we have agreements with two manufacturers, and one manufacturer provided commercial supplies of the product during 2018.

Kristalose®

We have an agreement for the purchase of Kristalose API with an international supplier. We also have manufacturing relationships with two packagers who provided finished supplies of the product for commercial and sampling purposes during 2018.

Omeclamox-Pak®

Prior to our asset purchase agreement with GEL that closed in December 2018, GEL managed the packaging and supply of Omeclamox-Pak commercial and sample units. Following our acquisition of the remaining rights to the brand in late 2018, we assumed responsibility for the packaging and supply of the product.

Vaprisol®

As part of the acquisition of Vaprisol, we purchased a significant existing supply of raw material inventory. In addition, as part of that transaction, we were assigned a commercial supply agreement with the historical Vaprisol manufacturer. In 2018, the manufacturer informed us that they would no longer be able to provide the product following the manufacturing of one final batch which is expected to provide us with a multi-year supply. Therefore, we are evaluating alternatives for a new manufacturer to provide us with long term supplies of the product.

Ethyol®

Under our Ethyol agreement, Clinigen is responsible for the supply of the product and has provided commercial inventory for Cumberland to package and distribute. Clinigen is in the process of establishing a new manufacturer for long term supplies of the product.

Totect®

As part of the Totect agreement, Clinigen is also responsible for overseeing the manufacture of the product and has provided commercial supplies for us to package and distribute.

Vibativ®

Through our acquisition of Vibativ, we acquired a multi-year supply of raw material, work in process and finished goods inventory. As a result of the agreement, we are now responsible for the future manufacture of the product and are in the process of completing the transfer of the product's manufacturing activities to a new supplier.

Distribution

Like many pharmaceutical companies, we engage a third-party with appropriate facilities and logistical expertise to support the U.S. distribution of our products. Cardinal Health has exclusively handled our U.S. product logistics activities, including warehousing, shipping, and various other customer activities. Our primary customers are the wholesalers of pharmaceuticals who provide our products to hospitals, clinics and retail pharmacies in the U.S.

CORPORATE DEVELOPMENT

Cumberland Foundation

In December 2017 we formed the Cumberland Pharma Foundation (the "Foundation") to serve as a vehicle to facilitate the ongoing philanthropic endeavors of Cumberland Pharmaceuticals Inc.

The Foundation was formed as an independent, nonprofit corporation designed to qualify as a tax-exempt organization pursuant to Section 501(a) of the Internal Revenue Code. The Foundation's Board of Directors was initially comprised of Cumberland Pharmaceuticals executives who are responsible for overseeing the Foundation's ongoing activities including charitable contributions.

We provided a grant of 50,000 shares of our common stock to the Foundation. The shares will address the ongoing financial needs of the Foundation, with most of the shares expected to be held for the opportunity to realize long term appreciation to support the Foundation's future. The Foundation will maintain independent financial statements and its contributions will not impact the financial statements of Cumberland Pharmaceuticals. Initial annual grants by the Foundation are expected to equal approximately 5% of the Foundation's total holdings, which is consistent with the historic level of contributions made by Cumberland Pharmaceuticals.

Cumberland Health and Wellness Political Action Committee

In November 2017 we formed the Cumberland Health and Wellness Political Action Committee (PAC). The objective of the PAC is to support candidates and policies that are consistent with Cumberland's mission of advancing patient care. The PAC's activities will be at the local, state and federal level and conducted in a bi-partisan manner. The initial committee membership is comprised of Cumberland Pharmaceuticals employees. The PAC received initial funding from us and future funding will include voluntary individual contributions from Cumberland Pharmaceuticals directors and employees.

SUBSEQUENT EVENTS

Next Generation Caldolor Product

In January 2019, the FDA approved our application of our next generation Caldolor (ibuprofen) injection product. In February 2018, Cumberland completed and filed with the FDA an application for approval. The product features a new, patented formulation in a more convenient to use package.

RediTrex Submission

In January 2019, we received notification from the FDA setting September 2019 as the Prescription Drug User Fee ("PDUFA") action date for an approval decision regarding the New Drug Application ("NDA") for our methotrexate product line. Our new line of methotrexate products is designed for the treatment of adult and pediatric patients with rheumatoid arthritis, as well as adults with psoriasis. The NDA was accepted for filing by the FDA in early January, following its submission to the FDA in November 2018.

PATENTS, TRADEMARKS AND OTHER INTELLECTUAL PROPRIETARY RIGHTS

We own the trademarks for each of our branded pharmaceutical products as well as for our corporate name and logo. We have applied for trademark registration for other various names and logos. Over time, we intend to maintain registrations on trademarks that remain valuable to our business.

We seek to protect our products from competition through a combination of patents, trademarks, trade secrets, FDA exclusivity and contractual restrictions on disclosure. Proprietary rights, including patents, are an important element of our business. We seek to protect our proprietary information by requiring our employees, consultants, contractors and other advisors to execute agreements providing for protection of our confidential information upon commencement of their employment or engagement. We also require confidentiality agreements from entities to which we provide our confidential information or materials.

Acetadote®

We developed a new formulation of Acetadote (acetylcysteine) Injection as part of a Phase IV commitment in response to a request by the FDA to evaluate the reduction of EDTA from the product's formulation. In April 2012, the USPTO issued U.S. Patent number 8,148,356 (the “356 Acetadote Patent”) which is assigned to us. The claims of the 356 Acetadote Patent encompass the new Acetadote formulation and include composition of matter claims. Following its issuance, the 356 Acetadote Patent was listed in the FDA Orange Book. The 356 Acetadote Patent is scheduled to expire in May 2026, which time period includes a 270-day patent term adjustment granted by the USPTO.

Following the issuance of the 356 Acetadote Patent, we received separate Paragraph IV certification notices from InnoPharma, Inc. ("InnoPharma"), Paddock Laboratories, LLC (“Paddock”), Mylan Institutional LLC (“Mylan”), Sagent Agila LLC ("Sagent") and Perrigo Company ("Perrigo") challenging the 356 Acetadote Patent on the basis of non-infringement and/or invalidity. We responded by filing five separate infringement lawsuits, in the appropriate United States District Courts, to contest each of the challenges.

On November 12, 2012, we entered into a Settlement Agreement (the “Settlement Agreement”) with Paddock and Perrigo to resolve the challenges and the pending litigation with those two companies. On November 1, 2013, the United States District Court filed opinions granting Sagent’s and InnoPharma’s motions to dismiss our suits and we agreed not to file an appeal or motion to reconsider, thereby resolving the challenges and the pending litigation with those two companies.

Under the Settlement Agreement, Paddock and Perrigo admit that the 356 Acetadote Patent is valid and enforceable and that any Paddock or Perrigo generic version of Acetadote (with or without EDTA) would infringe upon the 356 Acetadote Patent. In addition, Paddock and Perrigo will not challenge the validity, enforceability, ownership or patentability of the 356 Acetadote Patent through its expiration currently scheduled for May 2026. On November 12, 2012, in connection with the execution of the Settlement Agreement, we entered into a License and Supply Agreement with Paddock and Perrigo (the “License and Supply Agreement”).

Under the terms of the License and Supply Agreement, if a third party receives final approval from the FDA for an ANDA to sell a generic Acetadote product and such third party made such generic version available for purchase in commercial quantities in the United States, we are to supply Perrigo with an Authorized Generic version of our Acetadote product.

On May 18, 2012, we also submitted a Citizen Petition to the FDA requesting that the FDA refrain from approving any applications for acetylcysteine injection that contain EDTA, based in part on the FDA's request that we evaluate the reduction or removal of EDTA from our original Acetadote formulation.

On November 7, 2012, the FDA responded to the Citizen Petition denying our request and on November 8, 2012, we learned that the FDA approved the ANDA referencing Acetadote filed by InnoPharma, Inc. We brought suit against the FDA contesting the FDA's decision to approve the InnoPharma generic on November 13, 2012. On

September 30, 2013, the United States District Court filed an opinion granting a summary judgment in favor of the FDA regarding this suit.

As noted above, during 2012 the FDA approved the ANDA referencing Acetadote filed by InnoPharma, Inc. Upon this condition, in accordance with the License and Supply agreement with Perrigo, we began to supply Perrigo with our Authorized Generic. On January 7, 2013, Perrigo announced initial distribution of our Authorized Generic acetylcysteine injection product.

On March 19, 2013, the USPTO issued U.S. Patent number 8,399,445 (the “445 Acetadote Patent”) which is assigned to us. The claims of the 445 Acetadote Patent encompass the use of the 200 mg/ml Acetadote formulation to treat patients with acetaminophen overdose. On April 8, 2013, the 445 Acetadote Patent was listed in the FDA Orange Book. The 445 Acetadote Patent is scheduled to expire in August 2025. Following the issuance of the 445 Acetadote Patent we received separate Paragraph IV certification notices from Perrigo, Sagent Pharmaceuticals, Inc., and Mylan challenging the 445 Acetadote Patent on the basis of non-infringement, unenforceability and/or invalidity.

On June 10, 2013, we became aware of a Paragraph IV certification notice from Akorn, Inc. challenging the 445 Acetadote Patent and the 356 Acetadote Patent on the basis of non-infringement. On July 12, 2013, we filed a lawsuit for infringement of the 356 Acetadote Patent against Akorn, Inc. in United States District Court.

On February 18, 2014, the USPTO issued U.S. Patent number 8,653,061 (the “061 Acetadote Patent”) which is assigned to us. The claims of the 061 Acetadote Patent encompass the use of the 200 mg/ml Acetadote formulation to treat patients with acetaminophen overdose. Following its issuance, the 061 Acetadote Patent was listed in the FDA Orange Book. The 061 Acetadote Patent is scheduled to expire in August 2025.

On May 13, 2014, the USPTO issued U.S. Patent number 8,722,738 (the “738 Acetadote Patent”) which is assigned to us. The claims of the 738 Acetadote Patent encompass administration methods of acetylcysteine injection, without specification of the presence or lack of EDTA in the injection. Following its issuance, the 738 Acetadote Patent was listed in the FDA Orange Book and it is scheduled to expire in April 2032.

On December 11, 2014 and March 3, 2015, we became aware of Paragraph IV certification notices from Aurobindo Pharma Limited and Zydus Pharmaceuticals (USA) Inc., respectively, challenging the 356, 445, 061, and 738 Acetadote Patents on the basis of non-infringement.

On February 10, 2015, the USPTO issued U.S. Patent number 8,952,065 (the “065 Acetadote Patent”) which is assigned to us. The claims of the 065 Acetadote Patent encompass the use of the 200 mg/ml Acetadote formulation to treat patients with acute liver failure. The 065 Acetadote Patent is scheduled to expire in August 2025.

On September 30, 2015, the United States District Court for the Northern District of Illinois, Eastern Division ("District Court") ruled in our favor in our lawsuit against Mylan for infringement of the 445 Acetadote Patent. The opinion upheld our 445 Acetadote Patent and expressly rejected Mylan's validity challenge. The District Court ruled that Mylan is liable to us for infringement of the 445 Acetadote patent in light of Mylan's Abbreviated New Drug Application in which Mylan sought to market a generic version of Acetadote.

On November 17, 2015, the District Court entered an order enjoining Mylan and its affiliates from selling or using its generic version of Acetadote until August 2025, the date of expiration of the 445 Acetadote Patent. On October 30, 2015, Mylan filed a notice of appeal to the U.S. Court of Appeals for the Federal Circuit (the "Appeals Court").

On May 3, 2016, the USPTO issued U.S. Patent number 9,327,028 (the “028 Acetadote Patent”) which is assigned to us. The claims of the 028 Acetadote Patent encompass administration methods of acetylcysteine injection, without specification of the presence or lack of EDTA in the injection. Following its issuance, the 028 Acetadote Patent was listed in the FDA Orange Book and it is scheduled to expire in July 2031.

On January 26, 2017, the Appeals Court affirmed the District Court ruling in our favor in our lawsuit against