Akebia Therapeutics, Inc.
Form 10-K
March 26, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
Commission File Number 001-36352

AKEBIA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

| | |
|---|---|
| Delaware<br>(State or other jurisdiction of incorporation or organization) | 20-8756903<br>(I.R.S. Employer Identification No.) |
| 245 First Street, Cambridge, MA<br>(Address of principal executive offices) | 02142<br>(Zip Code) |

Registrant’s telephone number, including area code: (617) 871-2098

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

| Title of each class | Name of each exchange on which registered |
|---|---|
| Common Stock, par value $0.00001 per share | The Nasdaq Global Market |

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

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

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

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

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

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

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

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

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

Indicate by check mark whether 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, based on the closing price of the registrant's Common Stock on The Nasdaq Global Market on June 30, 2018, was $534,415,547.

The number of shares of registrant's Common Stock outstanding as of March 15, 2019 was 117,122,262.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Proxy Statement for the registrant's 2019 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

TABLE OF CONTENTS

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that are being made pursuant to the provisions of the U.S. Private Securities Litigation Reform Act of 1995 with the intention of obtaining the benefits of the "safe harbor" provisions of that Act. These forward-looking statements may be accompanied by words such as "anticipate," "believe," "build," "can," "contemplate," "continue," "could," "should," "designed," "estimate," "project," "expect," "forecast," "intend," "likely," "may," "plan," "possible," "potential," "predict," "strategy," "seek," "target," "will," "would," and other wo similar meaning. These forward-looking statements include, but are not limited to, statements about:

- our expectations with respect to (i) the anticipated financial impact and potential benefits to us related to our merger with Keryx Biopharmaceuticals, Inc., or Keryx, that was completed on December 12, 2018, or the Merger, (ii) integration of the businesses subsequent to the Merger, and (iii) other matters related to the Merger;
- the potential therapeutic applications of the hypoxia inducible factor, or HIF, pathway;
- our pipeline, including its potential, and our research activities;
- the potential therapeutic benefits, safety profile, and effectiveness of our product candidates, including the potential for vadadustat to set a new standard of care in the treatment of anemia due to chronic kidney disease;
- the potential indications and market potential and acceptance of our product and product candidates, including our estimates regarding the potential market opportunity for Auryxia, vadadustat or any other product candidates and the size of eligible patient populations;
- our competitive position, including estimates, developments and projections relating to our competitors and their products and product candidates, and our industry;
- our expectations, projections and estimates regarding our costs, expenses, revenues, capital requirements, need for additional capital, financing our future cash needs, capital resources, cash flows, financial performance, profitability, tax obligations, liquidity, growth, contractual obligations, the period of time our cash resources and collaboration funding will fund our current operating plan, internal control over financial reporting, and disclosure controls and procedures;
- the timing of the availability and disclosure of clinical trial data and results;
- our and our collaborators' strategy, plans and expectations with respect to the development, manufacturing, commercialization, launch, marketing and sale of our product candidates, and the associated timing thereof;
- the designs of our studies, and the type of information and data expected from our studies and the expected benefits thereof;
- the timing of or likelihood of regulatory filings and approvals, including labeling or other restrictions;
- our ability to maintain any marketing authorizations we currently hold or will obtain, including our marketing authorizations for Auryxia and our ability to complete post-marketing requirements with respect thereto;
- our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms and processes on a timely basis, or at all, with third-party payors for Auryxia or any other product candidate that may be approved;
- the targeted timing of enrollment of our clinical trials;
- the timing of initiation of our clinical trials and plans to conduct preclinical and clinical studies in the future;
- the timing and amounts of payments from or to our collaborators and licensees, and the anticipated arrangements and benefits under our collaboration and license agreements, including with respect to milestones and royalties;
- our intellectual property position, including obtaining and maintaining patents; and the timing, outcome and impact of administrative, regulatory, legal and other proceedings relating to our patents and other proprietary and intellectual property rights;
- expected reliance on third parties, including with respect to the development, manufacturing, supply and commercialization of our product and product candidates;
- accounting standards and estimates, their impact, and their expected timing of completion;

- estimated periods of performance of key contracts;
- our facilities, lease commitments, and future availability of facilities;
- cybersecurity;
- insurance coverage;
- our employees, including our management team, employee compensation, employee relations, and our ability to attract and retain high quality employees;
- the implementation of our business model, current operating plan, and strategic plans for our business, product candidates and technology, and business development opportunities including potential collaborations, alliances, mergers, acquisitions or licensing of assets;
- the timing, outcome and impact of current and any future legal proceedings.

These forward-looking statements involve risks and uncertainties, including those that are described in Part I, Item 1A. Risk Factors included in this Annual Report and elsewhere in this Annual Report on Form 10-K, that could cause our actual results, financial condition, performance or achievements to be materially different from those indicated in these forward-looking statements. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Forward-looking statements speak only as of the date of this Annual Report on Form 10-K. Except as required by law, we assume no obligation to publicly update or revise these forward-looking statements for any reason. Unless otherwise stated, our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

This Annual Report on Form 10-K also contains estimates and other information concerning our industry and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Unless otherwise expressly stated, we obtained this industry, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

In this Annual Report on Form 10-K, unless otherwise stated or the context otherwise requires, references to “Akebia,” “we,” “us,” “our,” “the Company,” and similar references refer to Akebia Therapeutics, Inc. and, where appropriate, its subsidiaries, including Keryx. The trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners. All website addresses given in this Annual Report on Form 10-K are for information only and are not intended to be an active link or to incorporate any website information into this document.

PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on the development and commercialization of therapeutics for patients with kidney disease. On December 12, 2018, we completed a merger, or the Merger, with Keryx Biopharmaceuticals, Inc., or Keryx, combining a nephrology-focused commercial organization with our robust development organization. Following the Merger, Keryx is our wholly owned subsidiary, and we are integrating our business and Keryx's business with the goal of positioning Akebia to realize the potential growth opportunities and synergies from the Merger.

We now have a commercial product and a late-stage product candidate:

- Auryxia® (ferric citrate) is approved and marketed in the United States for two indications: (1) the control of serum phosphorus levels in adult patients with chronic kidney disease, or CKD, on dialysis, or DD-CKD, or the Hyperphosphatemia Indication, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with CKD not on dialysis, or NDD-CKD, or the IDA Indication. Ferric citrate is also approved and marketed in Japan as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, under the trade name Riona® (ferric citrate hydrate) and approved in the European Union, or the EU, for the control of hyperphosphatemia in adult patients with CKD under the trade name Fexeric® (ferric citrate).
- Vadadustat is an investigational, oral hypoxia-inducible factor prolyl hydroxylase inhibitor, or HIF-PHI, in global Phase 3 development for two indications: (1) anemia due to CKD in adult patients with DD-CKD, and (2) anemia due to CKD in adult patients with NDD-CKD. We believe vadadustat has the potential to set a new oral standard of care for patients with anemia due to CKD, subject to regulatory approval. Vadadustat's proposed mechanism of action is designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with increased production of hypoxia-inducible factor, or HIF, which coordinates the interdependent processes of iron mobilization and stimulates endogenous production of erythropoietin, or EPO, to increase red blood cell, or RBC, production and, ultimately, improve oxygen delivery.

We market Auryxia in the United States with our well-established, nephrology-focused commercial organization. Our Japanese sublicensee, Japan Tobacco, Inc., or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize Riona in Japan. Fexeric is not currently marketed in the EU.

We plan to commercialize vadadustat, subject to U.S. Food and Drug Administration, or FDA, approval, in the United States with our commercial organization, while also leveraging our collaboration with Otsuka Pharmaceutical Co. Ltd., or Otsuka, and its U.S. commercial organization. We also granted Otsuka exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. In Japan and certain other countries in Asia, we granted Mitsubishi Tanabe Pharma Corporation, or MTPC, exclusive rights to commercialize vadadustat, subject to marketing approvals. In addition, we granted Vifor (International) Ltd., or Vifor Pharma, an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, which manages approximately 40% of the dialysis patients in the United States, at its U.S. dialysis clinics, subject to FDA approval of vadadustat, vadadustat's reimbursement under a bundled reimbursement model, and a milestone payment by Vifor Pharma.

Strategy

Our goal is to become a leading biopharmaceutical company focused on the treatment of patients with kidney disease, through the discovery, development and commercialization of innovative therapeutics. The key elements of our strategy are as follows:

- Maximize commercial opportunity for Auryxia. We aim to gain market share in Auryxia's Hyperphosphatemia Indication by leveraging Auryxia's product profile and opportunities for adoption following the release of updated clinical guidelines. We aim to gain market share and grow the market for Auryxia's IDA Indication by offering an alternative to the existing treatment approach.
- Complete global development and commercialization of our late-stage product candidate, vadadustat. We believe vadadustat has the potential to address limitations of injectable erythropoiesis-stimulating agents, or ESAs, and set a new standard of care for the treatment of anemia due to CKD, subject to regulatory approval. We are conducting a global Phase 3 clinical development program for vadadustat, and our collaboration partner, MTPC, is conducting a Phase 3 clinical development program for vadadustat in Japan. We believe we are well positioned to commercialize vadadustat in the United States in partnership with Otsuka and through our agreement with Vifor Pharma, subject to FDA approval. We plan to support Otsuka's and MTPC's commercialization of vadadustat in Europe, China and certain other markets, subject to regulatory approvals. We retained full commercial rights to vadadustat in Latin America, allowing us maximum flexibility in the region.

- Leverage portfolio synergies between our product, Auryxia, and our product candidate, vadadustat, in CKD. We believe there is an opportunity to maximize the U.S. commercial performance of Auryxia and vadadustat, subject to FDA approval and launch, by leveraging our nephrology-focused commercial organization for Auryxia and our relationships and expertise in the renal space. We also plan to explore co-development potential for Auryxia and vadadustat.
- Expand our pipeline and portfolio of renal therapeutics to advance care for patients with kidney disease. We aim to add to our pipeline and portfolio of renal therapeutics through internal discovery and development, and through strategic transactions, such as in-licenses, collaborations and acquisitions. Our pipeline and portfolio expansion efforts will be guided by our vision to improve the health of patients with kidney disease through better disease management and novel therapeutics.

Our management team has extensive experience in developing and commercializing drugs for the treatment of renal and metabolic disorders, a deep understanding of the renal space and biological pathways involved in kidney disease including HIF biology, and broad business development expertise. With this management team, fully integrated capabilities spanning research, manufacturing, development and commercialization, a growing revenue stream and a strong balance sheet, we are well positioned to execute on our strategy.

Kidney Disease

Kidney disease is an area of major unmet need globally, driving massive healthcare costs and with a generally poor prognosis: eventually many patients will progress to a stage where they are dependent on dialysis, with high morbidity and a significant increase in mortality rate.

Kidney disease can be caused by a number of distinct and concomitant factors, including cardiometabolic disorders (primarily diabetes and hypertension), genetic kidney diseases, autoimmune disorders, and aging. Given the prevalence and growth rates of these various underlying conditions, kidney disease prevalence is expected to continue to increase globally. In the United States, kidney disease significantly impacts the U.S. healthcare system, affecting more than 40 million patients and costing Medicare over $110 billion annually in 2016 for the care provided in dialysis clinics, nephrology centers and hospitals. The U.S. Department of Health and Human Services has recognized the national pandemic and partnered with the American Society of Nephrology to found the KidneyX Innovation Accelerator, a public-private partnership to improve the lives of the 850 million people worldwide currently affected by kidney diseases by accelerating innovation in the prevention, diagnosis and treatment of kidney diseases.

Most of the conditions covered by the term “kidney disease” may ultimately lead to dependence on dialysis or kidney transplant for survival, causing renal failure, directly or indirectly, by accelerating the onset of CKD. Dependence on dialysis is associated with a significant increase in mortality and hospitalizations, and a significant reduction in quality of life for patients. It is our vision, in time, to provide or contribute to better alternatives for patients with kidney disease.

As a first step towards our vision, we aim to advance care for patients with CKD, which is the current focus of our pipeline and our FDA-approved product, Auryxia.

CKD is a condition in which the kidneys are progressively damaged to the point that they cannot properly filter the blood circulating in the body. This damage causes waste products to build up in the patient’s blood leading to other health problems, including anemia, cardiovascular disease and bone disease. As illustrated in the table below, CKD patients are categorized in one of five stages based on the degree of their loss of kidney function as measured by the glomerular filtration rate, or GFR, and the level of protein in the urine, referred to as albuminuria. CKD is estimated to affect approximately 37 million adults in the United States.

Stages and Prevalence of Chronic Kidney Disease in the United States

| Stage | Description | GFR (mL/min/1.73m$^2$)[a] | U.S. Prevalence Rates[b, c] | Estimated Number of U.S. Patients (millions)[d, e] |
|---|---|---|---|---|
| 1 | Kidney damage with normal or increased GFR | ≥90 | 4.6% | 11.2 |
| 2 | Kidney damage with mildly decreased GFR | 60-89 | 3.0% | 7.3 |
| 3 | Moderately decreased GFR | 30-59 | 6.7% | 16.4 |
| 4 | Severely decreased GFR | 15-29 | 0.4% | 1.0 |
| 5 | Kidney failure (includes non dialysis, dialysis and transplant) | <15 (or dialysis) | 0.3% (calculated) | 0.7 |

5

Sources:

[a] GFR categories defined in the August 2012 Kidney Disease Improving Global Outcomes Clinical Practice Guideline for Anemia in Chronic Kidney Disease, p. vii.
[b] U.S. Prevalence Rates for Stages 1-4 based on averages of data from 2011-2012 and 2013-2014, CDC CKD Surveillance System, National Health and Nutrition Examination Survey, or NHANES.
[c] U.S. Prevalence Rate for Stage 5 is based on a calculation using estimated number of U.S. patients with Stage 5 CKD from 2017 U.S. Renal Data System Annual Report, as set forth in this table, and U.S. population data for people 20 years and older from www.census.gov.
[d] Estimated Number of U.S. Patients for Stages 1-4 based on the 2017 U.S. Prevalence rates, as set forth in this table, as applied by Akebia to U.S. population data for people 20 years and older from www.census.gov.
[e] Estimated Number of U.S. End-Stage Renal Disease Patients from 2017 U.S. Renal Data System Annual Report.

The prevalence and incidence of CKD is increasing in all segments of the United States population. Risk factors for the development of CKD include concomitant diseases such as hypertension, diabetes mellitus and cardiovascular disease, lifestyle factors such as tobacco use and inactivity, family history, aging and prenatal factors such as maternal diabetes mellitus, low birth weight and small-for-gestational-age status. According to an article in The Lancet published in May 2013, projected worldwide population changes suggest that the potential number of cases of CKD, specifically end-stage, will increase disproportionately in countries such as Japan, China and India where the number of elderly people is increasing. This effect will be accelerated further if the growth in the prevalence of hypertension and diabetes persists, along with the associated increased risk of stroke and cardiovascular disease, and access to treatment does not improve.

The progression of CKD towards renal failure is complicated by multiple conditions which further deteriorate kidney function and the general health of patients if left untreated. Typically the prevalence of these conditions increases as CKD progresses. For instance, anemia is characterized by low hemoglobin levels and is typically associated with a worsening quality of life, increased hospitalizations and increased mortality. The prevalence of anemia increases with the severity of CKD from an estimated 20% in patients with Stage 3 NDD-CKD to an estimated 95% in patients with Stage 5 DD-CKD.

Anemia, or low hemoglobin/red blood count, in patients with CKD most commonly arises from two etiologies:

1. IDA: results from low levels of iron due to abnormal iron absorption and utilization in patients with CKD.
2. Anemia due to CKD: results from inadequate levels of EPO, a protein hormone synthesized by specialized cells in the kidney that stimulates production of red blood cells in the bone marrow. As renal function declines, the body progressively loses the ability to produce endogenous EPO.

IDA in adult patients with NDD-CKD is an FDA-approved indication for Auryxia, and anemia due to CKD in NDD-CKD and DD-CKD patients are the two indications being investigated in Phase 3 clinical trials for vadadustat.

Hyperphosphatemia is another condition associated with CKD that is characterized by elevated serum phosphorus levels and is also typically associated with a worsening of health including increased cardiovascular risk and increased mortality. Hyperphosphatemia in DD-CKD patients is also an FDA-approved indication for Auryxia.

In addition to these conditions that are the current focus of our pipeline and portfolio of approved indications, there are several other disorders that have deleterious consequences on patient’s health, including hypercalcemia, hyperkalemia, hyponatremia, hypernatremia, and hyperparathyroidism. These conditions are generally not well controlled, particularly in the later stages of CKD and as patients transition to dialysis.

We are considering opportunities for further development and co-development of Auryxia and vadadustat in CKD patients, including in patients with later stage NDD-CKD.

When considering the clinical and commercial opportunities in CKD, it is important to take note of the contrasting market dynamics between DD-CKD and NDD-CKD.

DD-CKD patients receive treatment for the various complications of CKD including anemia and hyperphosphatemia. Given the concentration of dialysis clinics in large networks, with DaVita and Fresenius Kidney Care accounting for nearly 80% of the dialysis population in the United States, treatment is usually driven by medical protocols that are rolled out across the entire network of clinics. These protocols are informed by very large data sets and when updated, result in rapid change applicable to large segments of the patient population. This is particularly true of medications covered under the End Stage Renal Disease, or ESRD, Prospective Payment System, or PPS, in Medicare, or the ESRD Bundle, a payment structure with a flat base rate per dialysis session adjusted for individual patient and facility characteristics. Dialysis-related drugs are included in the ESRD Bundle if they fall into functional categories such as anemia management and bone and mineral metabolism, except that oral-only drugs are exempted from inclusion until 2025. In a final ESRD PPS rule published in November 2018, CMS confirmed that it will expand the Transitional Drug Add-On Payment Adjustment, or TDAPA, to all new dialysis drugs approved by the FDA after January 1, 2020. The TDAPA will provide separate payment for new drugs for two years based on the drug's Average Sales Price, ASP, that will be added to the base rate in order to facilitate the adoption of innovative therapies. Although there are several details that need clarification, the rule provides support for our assumption that new anemia treatments, including the HIF-PHI class, will be included in the ESRD Bundle and will be eligible for separate payment initially under TDAPA.

In contrast, NDD-CKD is characterized by larger patient populations with lower treatment rates for CKD-related conditions. In addition to improving cardiovascular risk and quality of life, unmet need includes delaying the progression of CKD and therefore the transition to dialysis. Reimbursement in the non-dialysis setting aligns with traditional commercial and government payer reimbursement for outpatient drugs.

Our Commercial Product: Auryxia

Overview

Auryxia (ferric citrate) is a non-calcium, non-chewable, orally-administered tablet that was approved for marketing by the FDA in September 2014 as a phosphate binder for the Hyperphosphatemia Indication and was commercially launched in the United States shortly thereafter. In November 2017, Auryxia received marketing approval from the FDA for a second indication, the IDA Indication, and was commercially launched for this indication in the United States shortly thereafter.

In January 2014, our Japanese sublicensee, JT, received approval from the Japanese Ministry of Health, Labour and Welfare to market ferric citrate in Japan under the trade name Riona as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and was commercially launched in Japan shortly thereafter. In September 2015, we received approval to market ferric citrate in the EU under the trade name Fexeric for the control of hyperphosphatemia in adult patients with CKD. Fexeric was also approved in the EU as a New Active Substance, or NAS, which provides 10 years of data and marketing exclusivity in the EU. Fexeric is not currently marketed in the EU, and our EU marketing authorization for Fexeric will cease to be valid on December 23, 2019 unless we commence marketing Fexeric in the EU by that date. We are exploring commercialization opportunities with third parties for Fexeric.

We have licensed and sublicensed certain intellectual property rights covering Auryxia from Panion & BF Biotech, Inc., or Panion. For more information regarding our intellectual property rights to Auryxia and our license agreement with Panion see Part I, Item 1. Business – Intellectual Property – Auryxia and Part I, Item 1. Business - License, Collaboration and Other Strategic Agreements – License Agreement with Panion & BF Biotech, Inc. We have received

four Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the FDA, with the first having been received on October 31, 2018. For more information about these Paragraph IV certification notice letters and any related litigation, see Part I, Item 3. Legal Proceedings.

Market Opportunity

Hyperphosphatemia

Hyperphosphatemia is a metabolic disorder characterized by elevated serum phosphorus levels. Phosphorus is a vital element required for most cellular processes and, in individuals with normal kidney function, excess dietary phosphorus is removed by the kidneys and excreted in urine. In adults with functioning kidneys, normal serum phosphorus levels are 2.5 to 4.5 mg/dL. In adults with DD-CKD, elevated phosphorus levels, or hyperphosphatemia, can be associated with adverse effects, including increased risk for cardiovascular disease, bone disease and death.

Phosphate binders are the only interventions marketed for the treatment of hyperphosphatemia. According to the U.S. Renal Data System, or USRDS, 2018 Annual Data Report, there are approximately 511,000 adult patients in the United States with DD-CKD in 2016, of which approximately 85% were treated with a phosphate binder. Phosphate binders need to be taken with meals and snacks, and it is not uncommon for DD-CKD patients to be prescribed as many as 12 or more phosphate binder pills per day, among other medications. Patients taking phosphate binders also experience gastrointestinal tolerability issues. As a result of the pill burden and tolerability issues associated phosphate binders, prescribed phosphate binders are often intolerable for many patients, leading to lack of treatment adherence and compliance.

In addition, in 2016 approximately 55% of patients treated with a phosphate binder were treated with a calcium-based binder, which can lead to side effects such as increased cardiovascular risk, hypercalcemia and gastrointestinal-related adverse events. Due to the risks associated with calcium-based binders, in 2017 Kidney Disease: Improving Global Outcomes, or KDIGO, recommended that clinicians limit the use of calcium-based binders. A third party market research survey of 195 nephrologists conducted in the fourth quarter of 2018 after the release of the 2017 KDIGO guidelines indicated that 51% of those surveyed anticipate decreasing their use of calcium-based binders in patients with DD-CKD.

Lanthanum-based phosphate binders are another alternative. Lanthanum is a rare earth element and is minimally absorbed in the gastrointestinal tract. Lower level tissue deposition, particularly in bone and liver, has been observed in animals, however, the long-term, potentially harmful, effects due to the accumulation of lanthanum in these tissues have not been clearly determined.

Aluminum-type phosphate binders were widely used in the past. However, the systemic absorption of aluminum from these agents and the potential toxicity associated with their use no longer make this type of binder a viable long-term treatment option.

Iron Deficiency Anemia

Anemia is a condition characterized by abnormally low levels of hemoglobin. Hemoglobin is contained within RBCs and carries oxygen to other parts of the body. If there are too few RBCs or if hemoglobin levels are low, the cells in the body will not get enough oxygen. IDA is a common form of anemia that is caused by patients not having enough iron to manufacture healthy RBCs. Although anyone can develop IDA, IDA is particularly common in patients with NDD-CKD. IDA is associated with fatigue, lethargy, decrease quality of life, cardiovascular complications, hospitalizations and increased mortality.

We estimate that there are more than 500,000 adult patients in the United States with NDD-CKD diagnosed with IDA. Currently, there are two forms of iron therapy used to treat IDA: oral iron supplements and iron delivered via intravenous infusion, or IV iron. Oral iron is currently the first-line iron replacement therapy for most physicians; however, oral iron supplements are poorly absorbed by many patients, which may adversely impact their effectiveness, and are associated with certain side effects, such as constipation, diarrhea and cramping, that may adversely affect patient compliance. IV iron is viewed as an effective treatment; however, like other intravenous medicines, it is logistically difficult to administer in an office setting, where NDD-CKD patients are more often treated.

Commercialization

We are marketing Auryxia in the United States through our well-established, nephrology-focused sales force and commercial organization. In 2018, our sales force called on approximately 7,300 nephrologists, who represented 82% of prescriptions written for phosphate binders by nephrologists.

Auryxia, as an oral drug, is covered by Medicare only under Part D. We have gained broad access for Auryxia in the United States in both Medicare Part D and commercial channels. Auryxia is currently covered for the Hyperphosphatemia Indication in nine of the ten largest Medicare Part D plans, which provide coverage for approximately 33.6 million people, and the ten largest commercial plans and pharmacy benefit managers in the United States, which provide coverage for approximately 131.7 million people. In September 2018, the Centers for Medicare & Medicaid Services, or CMS, decided that Auryxia would not be covered by Medicare for the IDA Indication. While this decision does not impact CMS coverage of the Hyperphosphatemia Indication, it requires all prescriptions for Auryxia for Medicare patients to undergo a prior authorization to ensure their use in the Hyperphosphatemia Indication. We are engaged in discussions with CMS and Medicare Part D sponsors on this matter as we believe that Auryxia should qualify for coverage under Medicare Part D of the CMS regulations for the IDA Indication.

JT, and its subsidiary, Torii, market Riona in Japan. We receive tiered double-digit royalties from JT and Torii based on their sales in Japan. Fexeric is not currently marketed in the EU, and our current marketing authorization for Fexeric in the EU ceases to be valid on December 23, 2019 unless we commence marketing Fexeric in the EU by that date. We are exploring commercialization opportunities with third parties for Fexeric.

Our Late-Stage Product Candidate: Vadadustat

Overview

Vadadustat is an investigational oral HIF-PHI product candidate, in global Phase 3 development for two indications: anemia due to CKD in adult patients with DD-CKD, and anemia due to CKD in adult patients with NDD-CKD. We believe vadadustat has the potential to set a new oral standard of care for patients with anemia due to CKD. Vadadustat's proposed mechanism of action is designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with increased production of HIF, which coordinates the interdependent processes of iron mobilization and EPO production to increase RBC production and, ultimately, improve oxygen delivery. The significance of the HIF pathway was recognized by the 2016 Albert Lasker Basic Medical Research Award, which honored the three physician-scientists who discovered the HIF pathway and elucidated this primary oxygen sensing mechanism that is essential for survival.

Market Opportunity

Anemia due to Chronic Kidney Disease

Anemia is common in patients with CKD, and its prevalence increases with disease progression. Anemia due to CKD results from inadequate EPO levels, which negatively affect RBC production. Left untreated, anemia accelerates overall deterioration of patient health with increased morbidity and mortality. Based on third party prevalence data and company estimates, approximately 37 million people in the United States have CKD and approximately 5.7 million of these individuals suffer from anemia. Anemia due to CKD is currently treated by injectable recombinant human ESAs, such as EPOGEN® (epoetin alfa) and Aranesp® (darbepoetin alfa), or blood transfusion. Based on publicly available information on ESA sales and market data compiled by a third-party vendor, global sales of injectable ESAs for all uses were estimated to be approximately $6.1 billion in 2018. The vast majority of these sales were for the treatment of anemia due to CKD.

When administered to a patient, injectable ESAs provide supraphysiological levels of exogenous EPO to stimulate production of RBCs. While injectable ESAs can be effective in raising hemoglobin levels, they have the potential to cause significant side effects, and need to be injected subcutaneously or intravenously. In particular, injectable ESAs may lead to thrombosis, stroke, myocardial infarction and death. These safety concerns, which became evident starting in 2006, have led to a significant reduction in the use of injectable ESAs. Data from the USRDS 2015 Annual Data Report indicate that the collective injectable ESA treatment rate in NDD-CKD patients in the United States decreased by approximately half from 2009 to 2013. Today, anemia is either not treated or inadequately treated in the majority of NDD-CKD patients.

According to the USRDS 2018 Annual Data Report, there were approximately 511,000 patients in the United States on dialysis in 2016, of which 88% were on in-center hemodialysis and the remainder on peritoneal or home hemodialysis. ESAs are given to approximately 90% of in-center hemodialysis patients and 75% of peritoneal dialysis patients. There is an unmet need for treatment options for patients with anemia due to CKD that offer an improved safety profile, and such agents would have significant market potential.

Vadadustat Has the Potential to Set a New Standard of Care

We believe that, based on the HIF-PHI mechanism of action and clinical data to date, vadadustat has the potential to set a new standard of care for the treatment of anemia due to CKD. Below is a summary of the key clinical findings;

further details are included below.

- Vadadustat stimulated endogenous EPO production. In two Phase 1 studies in normal healthy volunteers and one Phase 2 study in CKD patients, vadadustat increased serum EPO levels in a dose-dependent manner. Pre-dose EPO levels returned to baseline levels prior to subsequent daily dose. In these studies, vadadustat stimulated endogenous EPO production while avoiding supraphysiologic EPO levels.
- Vadadustat significantly increased and maintained hemoglobin levels. Our Phase 2 studies in CKD subjects with anemia demonstrated that vadadustat significantly increased and/or maintained hemoglobin levels.

- Vadadustat was dosed orally once daily and three times weekly. Our Phase 2 studies showed that vadadustat can be orally dosed once daily in NDD-CKD subjects with up to 20 weeks of dosing. In addition, our Phase 2 clinical study in DD-CKD subjects demonstrated that in subjects who remained on therapy, once daily oral dosing of vadadustat maintained stable hemoglobin levels in subjects converting from injectable ESA therapy over 16 weeks. This study also showed the potential for three-times weekly dosing of vadadustat in DD-CKD.
- Vadadustat resulted in favorable changes in iron parameters. In three Phase 2 clinical studies, treatment with vadadustat was associated with decreases in ferritin and hepcidin and increases in total iron binding capacity. These changes are consistent with improved iron mobilization and utilization for erythropoiesis in NDD-CKD and DD-CKD subjects.

Vadadustat has the potential to stimulate erythropoiesis, avoid supraphysiologic EPO levels, and possibly reduce risk of cardiovascular and thrombotic events associated with injectable ESAs. The efficacy of vadadustat in raising/maintaining hemoglobin levels and the cardiovascular safety of vadadustat as compared with darbepoetin alfa, an injectable ESA, is being assessed in the global Phase 3 clinical program for vadadustat.

Vadadustat Clinical Development – Phase 1 and Phase 2

We have completed twenty-two Phase 1 and Phase 2 studies of vadadustat. These studies included healthy volunteers, NDD-CKD and DD-CKD patients, and support continued development of vadadustat.

Findings from three Phase 2 studies demonstrated that vadadustat administered daily raised and/or maintained hemoglobin levels and improved markers of iron mobilization to support erythropoiesis in CKD patients. The range of doses used in these Phase 2 studies had been previously shown, in Phase 1 studies of healthy volunteers, to stimulate endogenous EPO production while avoiding supraphysiologic EPO levels. The results from one completed Phase 1 and two Phase 2 of these studies are summarized below.

Phase 1 Study in Normal Healthy Volunteers (CI-0002)

We completed a Phase 1 randomized, double-blind, placebo-controlled, multiple-ascending dose study to evaluate the safety, tolerability, pharmacodynamics response, and pharmacokinetics of vadadustat administered for 10 days to healthy male volunteers. Dose responsive increases in reticulocytes, or immature RBCs, and hemoglobin levels were demonstrated in the study. Mean serum EPO levels increased by 36%, 48%, and 89% over baseline, at 8 to 16 hours after dosing in the vadadustat 500 mg/day, 700 mg/day, and 900 mg/day dosing groups, respectively, and returned to baseline by 24 hours after dosing. The incidence of adverse events, or AEs, was generally similar between the combined vadadustat dosing groups, which was 76.5%, and the placebo group, which was 78%. Gastrointestinal AEs occurred in 26.5% of subjects in the vadadustat groups and in no subjects on placebo, of which mild to moderate diarrhea was the most frequent AE (24%), with evidence of a dose-related effect. No serious adverse events, or SAEs, or deaths were reported in this study.

Phase 2b Study in Non-Dialysis CKD Subjects (CI-0007)

We completed a multi-center Phase 2b study of vadadustat in non-dialysis subjects with anemia due to CKD. This double-blind, randomized, placebo-controlled study evaluated the efficacy and safety of vadadustat over 20 weeks of dosing in 210 subjects (138 vadadustat and 72 placebo) with CKD Stages 3 to 5. Subjects were enrolled into one of three groups: (1) injectable ESA naïve with hemoglobin ≤10.5 g/dL, (2) previously treated with injectable ESA with hemoglobin ≤10.5 g/dL, or (3) actively treated with injectable ESA with hemoglobin ≥9.5 and ≤12.0 g/dL, and were randomized at a ratio of 2 to 1 to once daily vadadustat or placebo. The primary endpoint was the percentage of subjects with either a mean hemoglobin of ≥11.0 g/dL or an increase in hemoglobin by ≥1.2 g/dL from baseline. A

protocol-defined dose adjustment algorithm was used to achieve the primary endpoint and to minimize hemoglobin excursions ≥13 g/dL.

The average age of subjects was 66 years; 78% of subjects had diabetes mellitus; and the mean estimated GFR was 25 mL/min/1.73m$^2$. 54.9% of vadadustat treated subjects compared to 10.3% of placebo treated subjects met the primary endpoint (p=0.0001). Only 4.3% of subjects in the vadadustat group had any hemoglobin excursion ≥13.0 g/dL. Between Groups 1 and 2 (the two correction cohorts; ESA-naïve and ESA previously treated), mean Hb increased significantly in the vadadustat group from pre-dose average to end-of-study average (Week 19/20). In Group 3 (conversion cohorts; ESA actively treated), placebo treated subjects experienced a decline in the mean hemoglobin within the first two weeks, whereas subjects randomized to vadadustat maintained a stable hemoglobin throughout the study.

Increases in hemoglobin in the vadadustat group were preceded by an increase in reticulocytes and accompanied by an increase in total iron binding capacity and a decrease in serum hepcidin and ferritin. There was no difference between the vadadustat and placebo groups in vascular endothelial growth factor, or VEGF, levels during the study.

A similar percentage of subjects experienced an AE in the vadadustat and placebo treatment groups (vadadustat 74.6% vs. placebo 73.6%); however, the frequency of certain AEs - diarrhea, nausea, hypertension and hyperkalemia - was greater in the vadadustat arm compared to placebo. In the vadadustat arm, a higher number of subjects reported SAEs of acute and chronic renal failure compared to placebo (9.4% vs. 2.8%, respectively); however, none was considered drug-related by the investigator. The percentage of subjects who had an SAE resulting in dialysis initiation, considered to be a more objective measure of the severity of renal disease, was comparable between vadadustat and placebo groups (8.0% versus 9.7%, respectively) and the number of subjects who discontinued from the study due to AEs of worsening CKD requiring dialysis was also comparable between the vadadustat (4.3%) and placebo (5.6%) groups. One subject with multiple co-morbidities and concomitant medications, including chlorthalidone, had an SAE of liver function test, or LFT, abnormal, considered a case of drug-induced liver injury meeting the biochemical criteria of Hy's Law, which was assessed as probably related to vadadustat. This subject made a complete recovery after vadadustat was discontinued. There were three deaths in vadadustat-treated subjects of which two cardiovascular deaths were considered to be unrelated to vadadustat and one death was attributed to myocardial ischemic and considered by the investigator to be possibly related to vadadustat; no autopsy was performed. There were no deaths in the placebo group.

In summary, vadadustat achieved the desired outcomes of raising and maintaining hemoglobin and increasing iron mobilization, while minimizing hemoglobin excursions ≥13 g/dL. Pergola et al published the results of this study in Kidney International 2016.

Phase 2 Study in Dialysis-Dependent CKD Subjects (CI-0011)

We completed a multi-center, open-label, 16-week study to assess the hemoglobin response, safety, and tolerability of vadadustat in DD-CKD subjects. The study enrolled 94 hemodialysis subjects with baseline hemoglobin levels of 9-12 g/dL, who were maintained on injectable ESAs prior to study entry. Subjects were converted from injectable ESA to vadadustat, and assigned to one of three dose cohorts: 300 mg once daily; 450 mg once daily; or 450 mg three-times weekly. For each dose cohort, the average hemoglobin level at study entry was compared to the average hemoglobin level at weeks 7 and 8, and to the average hemoglobin level at weeks 15 and 16. To evaluate hemoglobin response to each of the dose regimens, during the first eight weeks of this study, subjects were to remain on the prescribed starting dose, or decreased if necessary to control hemoglobin in the target range. Beginning at week 8, the dose of vadadustat could be increased or decreased to maintain hemoglobin levels as needed. Intravenous iron use was allowed.

The underlying demographics and profiles of these CKD subjects were well-balanced across the three cohorts, and reflective of the United States DD-CKD population as reported in the literature. Average age was 58 years, with an average time on dialysis of 4.6 years. The most common cause of end-stage renal disease was diabetes mellitus and/or hypertension. Baseline hemoglobin levels were similar at 10.4-10.6 g/dL in all three cohorts and the serum ferritin levels indicated that the subjects were iron replete at study entry and throughout the study.

For subjects in all three dosing cohorts (converted from ESA) who completed the study, the primary endpoint of maintaining stable mean hemoglobin levels over 16 weeks was achieved. In the sensitivity analysis using last observation carried forward to account for early discontinuations, mean Hb levels remained stable in the 300 mg daily dose cohort and modest declines were observed in the 450 mg daily and 450 mg three-times weekly dose cohorts. Post-hoc analyses indicated that baseline pre-conversion ESA dose was inversely associated with mean change in hemoglobin. Consistent with previous studies, all three starting dose regimens suggested an improvement in iron mobilization, as reflected by increases in total iron binding capacity and serum iron, and decreases in serum ferritin and hepcidin levels. Only one subject in the 300 mg once daily cohort had a single hemoglobin excursion to 13.1 g/dL.

These data support further development of vadadustat daily dosing to assess its long-term safety and efficacy in subjects on hemodialysis. These data also support further investigation of three times weekly dosing of vadadustat.

Adverse events were balanced across the three cohorts with 83% of subjects with at least one AE. There were no discernible trends in the frequency of AEs or SAEs by dose cohort. The most frequently reported AEs were nausea and diarrhea, 11.7% and 10.6%, respectively, with no apparent dose relationship. The majority of AEs were mild or moderate in severity. SAEs were reported in 13 subjects, or 13.8%, including two subjects with acute myocardial infarction considered not related to vadadustat by the investigator. No SAEs were reported as related to vadadustat and no deaths occurred during the study. Haase et al published the results of this study in Nephrology Dialysis Transplantation 2018.

Vadadustat Clinical Program

The following chart summarizes the current clinical program for our product candidate, vadadustat, which is in Phase 3 development.

Phase 1 and Phase 2 data led us to the design of our Phase 3 clinical program for vadadustat. The vadadustat Phase 3 program in DD-CKD patients with anemia due to CKD, called INNO$_2$VATE, and in NDD-CKD patients with anemia due to CKD, called PRO$_2$TECT, is designed to enroll up to approximately 7,600 patients evaluating once daily oral dosing of vadadustat against an injectable ESA active comparator, darbepoetin alfa. The enrollment numbers and the completion of INNO$_2$VATE and PRO$_2$TECT will be driven by the accrual of major adverse cardiovascular events, or MACE.

In August 2016, the first patient was dosed in INNO$_2$VATE. We completed enrollment in the larger of the two INNO$_2$VATE studies, which enrolled 3,554 subjects, in February 2019, and we expect to complete enrollment in the smaller INNO$_2$VATE study, enrolling approximately 350 subjects, by April 2019. We anticipate completing the larger of the two INNO$_2$VATE studies in the first quarter of 2020, with completion of the smaller INNO$_2$VATE study and availability of top-line data expected in the second quarter of 2020, subject to the accrual of MACE.

The first patient was dosed in PRO$_2$TECT in December 2015. We expect full enrollment of PRO$_2$TECT in 2019. We anticipate reporting top-line data for the PRO$_2$TECT studies in mid-2020, subject to the accrual of MACE. As of December 31, 2018, we expect the remaining external aggregate contract research organization, or CRO, costs of INNO$_2$VATE and PRO$_2$TECT to be in the range of $190.0 million to $220.0 million.

In both the PRO$_2$TECT and INNO$_2$VATE Phase 3 programs, the primary efficacy endpoint is the mean change in hemoglobin between baseline and the primary evaluation period. Non-inferiority, or NI, is achieved if the lower bound of the 95% confidence interval for the between-group difference of the mean hemoglobin change does not fall below the pre-specified NI margin. Both the PRO$_2$TECT and INNO$_2$VATE programs will include the primary safety endpoint of the assessment of MACE, with a comparison of vadadustat to darbepoetin alfa. MACE is defined as the composite endpoint of all-cause mortality, non-fatal myocardial infarction, or non-fatal stroke. To assess MACE, a pooled analysis of time to first MACE event from the two Phase 3 studies in each program (PRO$_2$TECT and INNO$_2$VATE) will be performed. NI is achieved if the upper bound of the 95% confidence interval for the hazard ratio of vadadustat to darbepoetin alfa does not exceed the pre-specified NI margin. We obtained feedback from the United States and European regulatory authorities regarding the design of these programs.

In addition, we have initiated a Phase 2 clinical study of vadadustat, FO$_2$RWARD-2, which will evaluate a modified approach to once-daily and three-times weekly dosing, including assessment of a vadadustat starting dose based on pre-conversion ESA dose and higher titration doses of vadadustat (750 mg and 900 mg). We expect to initiate two additional Phase 3 clinical studies of vadadustat, EXPLO$_2$RE and TRILO$_2$GY-2, which will evaluate modified once daily and three times weekly dosing of vadadustat, respectively. We believe data from these studies could support registration of the modified approach to once daily dosing and supplemental registration of three times weekly dosing, and further characterize vadadustat and further strengthen our potential commercial position if vadadustat is approved for marketing.

We completed a series of clinical drug-drug interaction studies largely focusing on transporter pathways evaluating vadadustat as a victim (using probe inhibitors) or perpetrator (using probe substrates) of drug interactions. No meaningful drug interactions were observed with atorvastatin (P-gp/OATP1B1 substrate), pravastatin (OATP1B1/1B3 substrate), digoxin (P-gp substrate), furosemide (OAT1/OAT3 substrate), adefovir (OAT1 substrate), cyclosporine (P gp/BCRP/OATP inhibitor), probenecid (OAT3 and UGT inhibitor), or rabeprazole (gastric acid-reducing agent). With concomitant administration of vadadustat, a mild-to-moderate interaction was observed with simvastatin (OATP1B1/B3 substrate), and moderate drug interactions were observed with rosuvastatin (BCRP/OATP1B1/1B3 substrate), ferrous sulfate, and sulfasalazine (BCRP substrate). In addition, in vitro drug-drug interaction studies demonstrated a very low risk of vadadustat for drug interactions due to alteration of metabolic enzyme activities, i.e. cytochrome P450 or UDP-glucuronosyltransferase isoforms. No clinical drug-interaction was observed with celecoxib (CYP2C9).

MTPC's Phase 3 Clinical Program of Vadadustat in Japanese Patients

On March 12, 2019, we announced positive top-line results from two Phase 3 active-controlled pivotal studies evaluating vadadustat in Japanese subjects with anemia due to CKD (J01 and J03 Studies). These studies were conducted by our development and commercialization collaboration partner in Japan, MTPC. Each study, one in non-dialysis dependent subjects and one in hemodialysis-dependent subjects, met its primary endpoint. In addition, results from two Phase 3 single-arm studies conducted by MTPC in peritoneal dialysis subjects and hemodialysis subjects (J02 and J04 Studies) further support vadadustat's potential in these indications. MTPC expects to submit a Japanese New Drug Application in 2019 for vadadustat for the treatment of anemia due to CKD.

The Phase 3 randomized, open-label, active-controlled correction and conversion study (J01 Study) assessed the efficacy and safety of vadadustat compared to darbepoetin alfa, an ESA, in 304 Japanese non-dialysis dependent subjects with anemia due to CKD, with a treatment duration of 52 weeks. Data from the planned analysis at 24 weeks are provided. The study met its primary endpoint, with the mean hemoglobin, or Hb, level at week 20 and week 24 at 11.66 g/dL (95% CI 11.49, 11.84 g/dL) for vadadustat-treated subjects compared to 11.93 g/dL (95% CI 11.76, 12.10 g/dL) for darbepoetin alfa-treated subjects. The difference in mean Hb was -0.26 g/dL (95% CI 0.50, -0.02 g/dL), achieving the pre-specified non-inferiority criterion of -0.75 g/dL. The incidence of adverse events, or AEs, was 72.2% in the vadadustat-treated group compared to 73.2% in the darbepoetin alfa-treated group. The most common AEs reported in vadadustat-treated subjects were nasopharyngitis (14.6%), diarrhea (10.6%), constipation (5.3%), and contusion (5.3%). The incidence of SAEs was 13.9% in the vadadustat-treated group compared to 14.4% in the darbepoetin alfa-treated group; no SAE was considered related to study drug. No deaths were reported in the vadadustat-treated group, and one fatal myocardial infarction was reported in the darbepoetin alfa-treated group, which was assessed as not related to study drug.

The Phase 3 randomized, double-blind, active-controlled conversion study (J03 Study) assessed the efficacy and safety of vadadustat compared to darbepoetin alfa in 323 Japanese hemodialysis subjects with anemia due to CKD who had been receiving ESA therapy prior to study screening, with a treatment duration of 52 weeks. Group level data at 24 weeks from this ongoing double-blind study are provided. The study met its primary endpoint, with the mean Hb level at week 20 and week 24 at 10.61 g/dL (95% CI 10.45, 10.76 g/dL) for vadadustat-treated subjects compared to

10.65 g/dL (95% CI 10.50, 10.80 g/dL) for darbepoetin alfa-treated subjects. The difference in mean Hb was -0.05 g/dL (95% CI -0.26, 0.17 g/dL), achieving the pre-specified non-inferiority criterion of -0.75 g/dL. The incidence of AEs was 89.5% in the vadadustat-treated group compared to 88.2% in the darbepoetin alfa-treated group. The most common AEs reported in vadadustat-treated subjects were nasopharyngitis (19.8%), diarrhea (10.5%), and shunt stenosis (8.0%). The incidence of SAEs was 13.0% in the vadadustat-treated group compared to 10.6% in the darbepoetin alfa-treated group; no SAE was considered related to study drug.

The Phase 3 open-label, single-arm study (J02 Study) assessed the efficacy and safety of vadadustat in 42 Japanese peritoneal dialysis subjects with anemia due to CKD, with a treatment duration of 24 weeks. The mean Hb level at week 20 and week 24 was 11.35 g/dL (95% CI 10.99, 11.70 g/dL) for vadadustat-treated subjects. Thirty-eight subjects (90.5%) experienced an AE and twelve (28.6%) experienced an SAE. One SAE of fatal myocardial ischemia was assessed as possibly related to vadadustat by the investigator.

The Phase 3 open-label, single-arm correction study (J04 Study) evaluated the safety and efficacy of vadadustat, with a treatment duration of 24 weeks, in 24 Japanese hemodialysis subjects with anemia due to CKD who had not been receiving ESA therapy prior to study screening or who underwent ESA washout during screening. The mean Hb level at week 20 and week 24 was 10.75 g/dL (95% CI 10.35, 11.14 g/dL) for vadadustat-treated subjects. Twenty-three subjects (95.8%) experienced an AE, and seven (29.2%) experienced an SAE. No SAE was assessed as related to study drug, and no deaths were reported.

Commercialization

We plan to commercialize vadadustat, subject to FDA approval, in the United States with our well-established, nephrology-focused commercial organization, while leveraging our collaboration with Otsuka and its U.S. commercial organization. We also granted Otsuka exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. In Japan and certain other countries in Asia, we granted MTPC exclusive rights to commercialize vadadustat, subject to marketing approvals. In addition, we granted Vifor Pharma an exclusive license to sell vadadustat solely to FKC, which manages approximately 40% of the dialysis patients in the United States, at its U.S. dialysis clinics, subject to FDA approval of vadadustat, vadadustat's reimbursement under a bundled reimbursement model, and a milestone payment by Vifor Pharma. During the term of the license agreement, Vifor Pharma may not sell to FKC or its affiliates any HIF product that competes with vadadustat in the United States. For more information about our license, collaboration and strategic agreements relating to vadadustat, see Part I, Item 1. Business – License, Collaboration and Other Strategic Agreements – Vadadustat.

Development Candidates

In addition to vadadustat, we are developing a HIF-based portfolio of other product candidates that target serious diseases of high unmet need. Our portfolio includes product candidates developed internally as well as in-licensed product candidates. In February 2017, we signed an exclusive agreement with Janssen Pharmaceutica NV, or Janssen, a subsidiary of Johnson & Johnson, or the Janssen Agreement, for access to an extensive library of well-characterized HIF pathway compounds with potential applications across multiple therapeutic areas. Our strategic focus will be to identify and develop candidates for kidney disease indications.

Manufacturing and Supply

Overview

We neither own nor operate, and currently have no plans to own or operate, any manufacturing or distribution facilities. We currently rely on third-party contract manufacturing organizations, or CMOs, to produce all of our preclinical and clinical material and commercial supply and third-party distributors to distribute Auryxia. We expect to continue to rely on either existing or alternative distributors and CMOs to distribute our products and supply our ongoing and planned preclinical and clinical studies and for commercial production.

We have established relationships with several CMOs under which the CMOs manufacture preclinical and clinical supplies of vadadustat drug substance and drug product and clinical and commercial supply of Auryxia drug substance and drug product. All clinical and commercial supplies are manufactured under current Good Manufacturing Practices, or cGMPs, which is a regulatory standard for the production of pharmaceuticals that will be used in humans.

Auryxia

We have established CMO relationships for the supply of Auryxia to help ensure that we will have sufficient material for clinical trials and ongoing commercial sales. The drug substance for Auryxia is supplied by Siegfried Evionnaz SA (two sites) and BioVectra Inc. (one site), pursuant to supply agreements with pricing structured on a per-kilogram basis. Auryxia drug product is supplied by Patheon Manufacturing Services LLC (Thermo Fisher) (three sites) pursuant to a Master Manufacturing Service Agreement with per-bottle pricing structured on a tiered basis, with the price reduced as the product volume increases. These agreements require that we satisfy certain minimum purchase requirements, but we are not obligated to use them as our sole suppliers. In addition, we are continuing to establish the basis for long-term commercial production capabilities to supply the potential expanded demand for Auryxia in future years. For more information about our manufacturing agreements for Auryxia, see Part II, Item 7. Management's

Discussion and Analysis and Note 16 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data.

As we continue to build inventory for the expanded commercialization of Auryxia, we intend to expand capacity to produce Auryxia under cGMP requirements. Our third party manufacturers have other clients and may have other priorities that could affect their ability to perform the work satisfactorily and/or on a timely basis. Both of these occurrences would be beyond our control.

Auryxia is a small molecule. The synthesis of Auryxia is reliable and reproducible from starting materials available from multiple sources at commercially relevant scale. Auryxia can be readily formulated into compressed tablets with standard ingredients using common manufacturing processes. As with any supply program, obtaining raw materials and finished drug product of the required quality and quantity cannot be guaranteed, and we cannot ensure that we will be successful in this endeavor.

We utilize third parties for the commercial distribution of Auryxia, including wholesale distributors and certain specialty pharmacy providers. We have also engaged Cardinal Health as the exclusive third-party logistics distribution agent for commercial sales of Auryxia.

Vadadustat

We currently have redundant supply arrangements in place for the preclinical and clinical supply of vadadustat. We intend to put supply agreements in place for commercial manufacturing of vadadustat in the near future. We plan to mitigate potential commercial supply risks for vadadustat, if any, through inventory management and redundant manufacturing arrangements for both drug substance and drug product; however, the timing of such arrangements is uncertain and may occur following the launch of vadadustat, if approved.

Vadadustat is a small molecule. The synthesis of vadadustat is reliable and reproducible from starting materials available from multiple sources at commercially relevant scale using no unusual manufacturing equipment. Vadadustat can be readily formulated into compressed tablets with standard ingredients using common manufacturing processes. As with any supply program, obtaining raw materials and finished drug product of the required quality and quantity cannot be guaranteed and we cannot ensure that we will be successful in this endeavor.

License, Collaboration and Other Strategic Agreements

Auryxia

License Agreement with Panion & BF Biotech, Inc.

In November 2005, Keryx entered into a license agreement with Panion. Under the license agreement, we acquired the exclusive worldwide rights, excluding certain Asian-Pacific countries, for the development, marketing and commercialization of ferric citrate. Under the agreement, Panion is eligible to receive from us milestone payments and royalty payments based on a mid-single digit percentage of net sales of ferric citrate in the licensed territory.

The license agreement terminates upon the expiration of our obligations to pay royalties thereunder. In addition, we may terminate the license agreement (i) in its entirety or (ii) with respect to one or more countries of the territory covered by the agreement, in either case upon 90 days' notice. We and Panion also have the right to terminate the license agreement upon the occurrence of a breach of a material provision of the license agreement, subject to certain cure provisions, or certain insolvency events.

On October 24, 2018, prior to the consummation of the Merger, we and Keryx entered into a letter agreement with Panion, the Panion Letter Agreement, pursuant to which Panion agreed to rescind any and all prior termination threats or notices relating to the license agreement and waived its rights to terminate the license agreement based on any breach by Keryx of our obligation to use commercially reasonable efforts to commercialize Auryxia outside the United States until the parties execute an amendment to the license agreement in accordance with the terms of the Panion Letter Agreement following consummation of the Merger. These terms include establishing a joint steering committee consisting of Panion and Akebia representatives to oversee the development and commercialization of Fexeric in Europe and providing Panion with an exclusive license under Keryx-owned patents covering the rights to make, use, sell, offer for sale and import ferric citrate in certain countries in the Asia-Pacific region. The parties intend to work together to agree on a commercialization plan for Fexeric in Europe following execution of the amendment. The amendment is expected to include alternatives in the event a commercialization plan is not agreed upon, such as payment of an annual license maintenance fee to Panion or the return of European intellectual property rights to Panion. Under the terms of the Panion Letter Agreement, Panion also agreed that we will have the right, but not the obligation, to conduct any litigation against any infringer of patent rights under the license agreement on the terms

agreed upon in the Panion Letter Agreement. In addition, Keryx made a $500,000 payment to Panion promptly after execution of the Panion Letter Agreement.

During the period from December 12, 2018 to December 31, 2018, Panion earned $0.4 million in royalty payments relating to the sales of Auryxia in the U.S. and JT and Torii net sales of Riona in Japan, as we are required to pay a low double-digit percent of sublicense income to Panion under the terms of the license agreement, excluding any income under the JT and Torii sublicense.

Sublicense Agreement with Japan Tobacco Inc. and Torii Pharmaceutical Co., Ltd.

In September 2007, Keryx entered into a Sublicense Agreement with JT and Torii, under which JT and Torii obtained the exclusive sublicense rights for the development and commercialization of ferric citrate in Japan. Effective June 8, 2009, Keryx entered into an Amended and Restated Sublicense Agreement, which was amended in June 2013, or the Revised Agreement, with JT and Torii, which, among other things, provided for the elimination of all significant on-going obligations under the Sublicense Agreement.

In January 2014, JT and Torii received manufacturing and marketing approval of ferric citrate from the Japanese Ministry of Health, Labour and Welfare. Ferric citrate, launched in May 2014 and being marketed in Japan by Torii under the brand name Riona, is indicated as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including NDD-CKD and DD-CKD. Under the terms of the license agreement with JT and Torii, we are eligible to receive royalty payments based on a tiered double-digit percentage of net sales of Riona in Japan escalating up to the mid-teens, subject to certain reductions upon expiration or termination of the Panion license agreement, and may also receive up to an additional $55.0 million upon the achievement of certain annual net sales milestones. In accordance with our revenue recognition policy, royalty revenues are recognized in the quarter that JT and Torii provide their written report and related information to us regarding sales of Riona, which generally will be one quarter following the quarter in which the underlying sales by JT and Torii occurred. We recorded $0.1 million in license revenue related to royalties earned on net sales of Riona in Japan during the period from December 12, 2018 to December 31, 2018. We record the associated mid-single digit percentage of net sales royalty expense due to Panion, the licensor of ferric citrate, in the same period as the royalty revenue from JT and Torii is recorded.

The sublicense terminates upon the expiration of all underlying patent rights. Also, JT and Torii may terminate the sublicense agreement with or without cause upon at least six months prior written notice to us. Additionally, either party may terminate the sublicense agreement for cause upon 60 days' prior written notice after the breach of any uncured material provision of the sublicense agreement, or after certain insolvency events.

Vadadustat

U.S. Collaboration with Otsuka Pharmaceutical Co. Ltd.

On December 18, 2016, we entered into a collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement, pursuant to which we agreed to co-exclusively collaborate with Otsuka with respect to the development and commercialization of vadadustat in the United States, subject to the approval of vadadustat by the FDA. We continue to lead the ongoing global Phase 3 development program for vadadustat. Under the Otsuka U.S. Agreement, subject to the terms of the Otsuka Funding Option, as described below, we control and retain final decision making authority with respect to, among other things, the development of vadadustat. Our obligations related to the conduct of the current global development plan include the associated manufacturing and supply services for vadadustat.

Under the terms of the Otsuka U.S. Agreement, Otsuka paid us an upfront payment of $125.0 million and we expect Otsuka to provide additional funding of $201.3 million or more, depending on the actual costs incurred, toward the vadadustat global Phase 3 development program. In addition, if the development costs exceed a certain threshold, or the Cost Threshold, then we may elect to require Otsuka to increase the aggregate percentage of the current global development costs it funds under the Otsuka U.S. Agreement and the Otsuka International Agreement, as defined below, from 52.5% to 80%, or the Otsuka Funding Option. In such event, the excess of the payments made under such election and Otsuka's allocated share of the current global development costs is fully creditable against future payments due to us under the arrangement, provided that future payments due to us may not be reduced by more than 50% in any calendar year and any remaining creditable amount above 50% in any calendar year will be applied to subsequent future payments until fully credited. In addition, decisions regarding certain development matters will be made jointly by us and Otsuka in accordance with the procedures set forth in the Otsuka U.S. Agreement. In September 2018, we exercised the Otsuka Funding Option, which will be effective when the Cost Threshold is exceeded. We estimate that the Cost Threshold will be exceeded in the second quarter of 2019. We are eligible to receive from Otsuka up to $190.0 million in development and regulatory milestones and up to $575.0 million in specified commercial milestones.

The Otsuka U.S. Agreement establishes a profit share for the commercialization of vadadustat in the United States. The parties will equally share all net sales of vadadustat in the United States, if approved, and each party will bear half

of all costs in the United States, including medical affairs, commercialization and manufacturing costs.

Under the Otsuka U.S. Agreement, we and Otsuka will jointly conduct, and will have equal responsibility for, all medical affairs and commercialization activities pursuant to plans agreed by the parties. We will remain responsible for manufacturing vadadustat. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the agreement.

International Collaboration with Otsuka Pharmaceutical Co. Ltd.

On April 25, 2017, we entered into a collaboration and license agreement with Otsuka, or the Otsuka International Agreement, pursuant to which we granted Otsuka an exclusive license for the development and commercialization of vadadustat in certain territory outside the United States. The territory covered by the Otsuka International Agreement includes the European Union, Russia, China, Australia, Canada, the Middle East and certain other countries, or the Otsuka International Territory, but excludes Latin America and previously licensed jurisdictions. Under the Otsuka International Agreement, Otsuka is responsible for certain development activities and commercializing vadadustat in the Otsuka International Territory, while we lead the ongoing global Phase 3 development program. Otsuka will fund a significant percentage of the costs of such global development program regardless of the total actual costs ultimately incurred. Subject to the terms of the Otsuka Funding Option, we retain final decision-making authority with respect to, among other things, the manufacture and supply of vadadustat in the Otsuka International Territory, the global Phase 3 development program, and the global brand strategy for vadadustat. Otsuka will have final decision-making authority with respect to certain development activities and commercialization matters in the Otsuka International Territory. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the agreement.

Under the terms of the Otsuka International Agreement, we expect Otsuka to pay us at least $249.3 million, comprised of $73.0 million that was paid upon execution of the Otsuka International Agreement and $176.3 million or more, depending on actual costs incurred, of development funding. In addition, we are eligible to receive from Otsuka up to $132.0 million in development and regulatory milestones and up to $525.0 million in commercial milestones, subject to reduction as described above. Otsuka also agreed to make tiered, escalating royalty payments ranging from low double digits up to thirty percent of net sales of vadadustat within the Otsuka International Territory. In limited circumstances, upper tier royalties may be subject to reduction if the supply price charged by us to Otsuka for vadadustat exceeds certain agreed upon thresholds, and royalty payments may also be reduced if a generic product is launched, on a country-by-country basis. Otsuka may elect to conduct additional studies of vadadustat in the European Union, subject to our right to delay such studies based on our objectives outside the Otsuka International Territory. Otsuka will pay a percentage of the costs of any such studies, and we will pay its portion of the costs in the form of a credit against future amounts due to us under the Otsuka International Agreement.

Collaboration with Mitsubishi Tanabe Pharma Corporation

On December 11, 2015, we entered into a collaboration agreement with MTPC, or the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to vadadustat in Japan and certain other Asian countries, or the MTPC Territory. In addition, we will supply vadadustat for both clinical and commercial use in the MTPC Territory, subject to MTPC’s option to manufacture commercial drug product in the MTPC Territory.

We and MTPC agreed that, instead of including Japanese patients in our global Phase 3 program for vadadustat, MTPC would be the sponsor of a Phase 3 program for vadadustat in Japan. Following consultation with the Japanese Pharmaceuticals and Medical Devices Agency, or the PMDA, MTPC initiated its Phase 3 development program for vadadustat in Japan in the fourth quarter of 2017.

Under the terms of the MTPC Agreement, MTPC will make payments to us of up to $245.0 million in the aggregate based on the achievement of certain development, regulatory and sales milestones, as well as tiered double-digit royalty payments of up to 20% on sales of vadadustat in the MTPC Territory, subject to reduction upon launch of a generic product on a country-by-country basis. MTPC is responsible for the costs of the Phase 3 program for vadadustat in Japan and will make no additional funding payments for our global Phase 3 program for vadadustat. Additionally, the development costs of approximately $20.5 million for our Phase 2 studies in Japan were reimbursed to us by MTPC, of which the last remaining $0.5 million was collected in the fourth quarter of 2018. We and MTPC

recently announced topline data from two pivotal Phase 3 clinical studies for vadadustat in Japan.

In addition, in September 2017 we agreed to provide MTPC with an option to access data from our global Phase 3 vadadustat program for payments to us of up to $25.0 million.

Vifor Pharma License Agreement

On May 12, 2017, we entered into a License Agreement with Vifor Pharma, or the Vifor Agreement, pursuant to which we granted Vifor Pharma an exclusive license to sell vadadustat solely to FKC, an affiliate of Fresenius Medical Care North America, in the United States, subject to the approval of vadadustat for DD-CKD patients by the FDA, inclusion of vadadustat in a bundled reimbursement model, and payment by Vifor Pharma of a $20 million milestone upon the occurrence of these two events. The Vifor Agreement is structured as a profit share arrangement between us and Vifor Pharma in which we will receive a majority of the profit from Vifor Pharma’s sales of vadadustat to FKC in the United States. We will share the milestone payment and the revenue from the profit share with Otsuka pursuant to the Otsuka U.S. Agreement. We retain all rights to commercialize vadadustat for use in the NDD-CKD market and in other dialysis organizations in the United States, which will be done in collaboration with Otsuka if approved by the FDA.

Prior and subject to FDA approval of vadadustat, we and Vifor Pharma plan to enter into a commercial supply agreement for vadadustat pursuant to which we would supply all of Vifor Pharma's commercial requirements for vadadustat in the United States. In addition, pursuant to the Vifor Agreement, Vifor Pharma entered into supply agreements that govern the terms pursuant to which Vifor Pharma would supply vadadustat to FKC for use in patients at its dialysis centers, subject to FDA approval; however, FKC is not obligated to utilize vadadustat in its clinics. During the term of the Vifor Agreement, Vifor Pharma will not sell to FKC or its affiliates any HIF product that competes with vadadustat in the United States.

Janssen Pharmaceutica NV Research and License Agreement

On February 9, 2017, we entered into a Research and License Agreement, the Janssen Agreement, pursuant to which Janssen granted us an exclusive license under certain intellectual property rights to develop and commercialize worldwide certain HIF-PH-targeted compounds.

Under the terms of the Janssen Agreement, Janssen granted us a license for a three-year research term to conduct research on Janssen's HIF compound portfolio, unless we elect to extend such research term for up to two additional one-year periods upon payment of an extension fee. During the research term, we may designate one or more compounds as candidates for development and commercialization. Once a compound is designated for development and commercialization, we will be solely responsible for the development and commercialization of the compound worldwide at our own cost and expense.

Under the terms of the Janssen Agreement, we paid an upfront payment of $1.0 million in cash to Janssen and issued a warrant to purchase 509,611 shares of our common stock, the fair value of which was approximately $3.4 million. In addition, Janssen could be eligible to receive up to an aggregate of $16.5 million from us in specified development milestone payments on a product-by-product basis. Janssen will also be eligible to receive up to $215.0 million from us in specified commercial milestones as well as tiered, escalating royalties ranging from a low to mid-single digit percentage of net sales, on a product-by-product basis and subject to reduction upon expiration of patent rights or the launch of a generic product in the territory.

Janssen also has a right of first offer to engage in exclusive negotiations with us to develop and commercialize certain products developed by us containing compounds for the treatment of inflammatory bowel disease.

Intellectual Property

The proprietary nature of, and protection for, our products, product candidates and our discovery programs, processes and know-how are important to our business. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. Additionally, we may benefit from a variety of statutory frameworks in the United States, Europe and other countries that provide periods of non-patent-based exclusivity for qualifying molecules. See "—Regulatory Matters."

Our commercial success will depend in part on obtaining and maintaining patent protection of our current products as well as current and future product candidates, methods of their use and the methods used to develop and manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products depends on the extent to which we have rights under valid and enforceable patents that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be

commercially useful in protecting our product candidates, discovery programs and processes. Even once patents successfully issue, third parties may challenge the validity, enforceability, inventorship, or scope thereof, which may result in such patents being narrowed, invalidated or held not infringed or unenforceable. For this and more comprehensive risks related to our intellectual property, please see “Risk Factors—Risks Related to Our Intellectual Property.”

Individual patents extend for varying periods of time depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued from applications filed in the United States are effective for 20 years from the earliest filing date of a United States non-provisional application or an international application filed under the Patent Cooperation Treaty. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, however, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest international filing date. Patent term recapture for loss of term as a result of the regulatory review period is available in some foreign jurisdictions. In the United States, a patent’s term may also 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 an earlier filed patent.

Changes in either the patent laws or interpretations of patent laws in the United States and other countries can diminish our ability to protect our inventions and enforce our intellectual property rights. Accordingly, we cannot predict the breadth or enforceability of claims that may be granted in our patents or in third-party patents. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to maintain and solidify our proprietary position for our drugs and technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of the patent applications that we may file or license from third parties will result in the issuance of any patents. The issued patents that we own or license or may receive or acquire in the future may be challenged, invalidated or circumvented, and the rights granted under any issued patents may not provide us with sufficient protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may be able to independently develop and commercialize similar drugs or duplicate our technology, business model or strategy without infringing our patents. Because of the extensive time required for clinical development and regulatory review of a drug we may develop, it is possible that, before any of our drugs can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent. The patent positions for Auryxia and vadadustast are summarized below.

Auryxia Patent Portfolio

Pursuant to our license with Panion & BF Biotech, Inc., or Panion, we have the exclusive rights under a series of patents and patent applications to commercialize Auryxia worldwide, excluding certain Asian-Pacific countries. These patents and patent applications include claims directed to compositions of matter, pharmaceutical compositions, methods of treatment, as well as methods for the manufacture of Auryxia.

Our patent rights include fourteen issued U.S. patents listed in the Orange Book covering the composition of matter, method of treating hyperphosphatemia, and pharmaceutical compositions of Auryxia. The expected expiration dates for these patents are between 2020 and 2030 plus any additional patent term extensions that may be available. These patents are currently being asserted against several generic companies for patent infringement. See Part I, Item 3. Legal Proceedings.

Pursuant to our sublicense with our Japanese partner, Japan Tobacco Inc., or JT, and its subsidiary, Torii Pharmaceutical Co. Ltd., or Torii, we have exclusively sublicensed certain Japanese patent rights to JT and Torii. These sublicensed rights include several Japanese patents and pending patent applications with composition of matter claims and methods of use claims covering Riona, the trade name under which JT and Torii market ferric citrate in Japan. The expected expiration dates for these patents are between 2022 and 2026. To date, to our knowledge, no contested proceedings or third-party claims have been lodged against any of these Japanese patents.

On November 25, 2015, a third party filed an opposition to our issued European Patent No. 1 931 689, or the ‘689 EP Patent, in the European Patent Office (“EPO”). During the oral proceedings, which took place on June 27, 2017, the Opposition Division of the EPO revoked the ‘689 EP Patent. On December 6, 2017, we filed an Appeal of the decision of the Opposition Division, which is presently pending. According to European practice, the revocation of the patent is stayed until an appeal is finally resolved. We anticipate the appeal will take a few years to resolve, during which time the patent will remain in force.

On December 23, 2016, a third party filed an opposition to our issued European Patent No. 1 978 807, or the ’807 EP Patent, in the EPO. During the oral proceedings, which took place on June 8, 2018, the Opposition Division of the EPO maintained the ’807 EP Patent as granted. This decision resulted in the maintenance of all the claims of the patent, including claims directed to the use of ferric citrate for preventing, reversing, maintaining or delaying progression of chronic kidney disease. On November 16, 2018, the third party filed an appeal of the decision of the Opposition Division, which is presently pending. We anticipate the appeal will take a few years to resolve.

Vadadustat Patent Portfolio

We hold eight issued patents covering the composition of matter, polymorph, method of treating anemia, and pharmaceutical compositions of vadadustat in the United States and additional patents issued or pending in many other major jurisdictions worldwide, including Europe, Japan, China, South Korea, Brazil, Mexico, Russia, Israel and India. The expected expiration dates for these patents are between 2027 and 2034 plus any extensions or adjustments of term available under national law.

In July 2011, a third party filed an opposition to our issued European Patent No. 2044005, or the ’005 EP Patent. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office maintained the ’005 EP Patent based on the third auxiliary request filed during the oral proceedings. This decision resulted in the maintenance of a claim directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases, including, but not limited to, anemia. Both parties appealed the decision of the Opposition Division. On February 27, 2018, we withdrew the ’005 EP Patent from appeal and filed a divisional patent application to pursue a focused claims set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia. We cannot be assured that such claims in the divisional patent application will be granted by the European Patent Office. If such claims are not granted, or the scope of the claims is significantly narrowed, we may not be able to adequately protect our rights, provide sufficient exclusivity, or preserve our competitive advantage.

In September 2018, Dr. Reddy’s Laboratories Limited filed an opposition to our issued Indian Patent No. 287720, or the ’720 IN Patent, in the Indian Patent Office.

We also hold patents and patent applications directed to processes for manufacturing vadadustat, dosing regimens, formulations, and various other aspects relating to the treatment of anemia using vadadustat that are expected to expire between 2032 and 2036 exclusive of possible patent term extensions or adjustments.

Other Intellectual Property Rights

We depend upon trademarks, trade secrets, know-how and continuing technological advances to develop and maintain our competitive position. To maintain the confidentiality of trade secrets and proprietary information, we require our employees, scientific advisors, consultants and collaborators, upon commencement of a relationship with us, to execute confidentiality agreements and, in the case of parties other than our research and development collaborators, to agree to assign their inventions to us. These agreements are designed to protect our proprietary information and to grant us ownership of technologies that are developed in connection with their relationship with us. These agreements may not, however, provide protection for our trade secrets in the event of unauthorized disclosure of such information.

In addition to patent protection, we may utilize orphan drug regulations, pediatric exclusivity or other provisions of the Food, Drug and Cosmetic Act of 1938, as amended, or FDCA, such as new chemical entity exclusivity or new formulation exclusivity, to provide market exclusivity for a drug candidate. In the United States, the FDA has the authority to grant additional data protection for approved drugs where the sponsor conducts specified testing in pediatric or adolescent populations. If granted, this pediatric exclusivity may provide an additional six months which are added to the term of data protection as well as to the term of a relevant patent, to the extent these protections have not already expired. We may also seek to utilize market exclusivities in other territories, such as in the EU. We cannot assure that our drug products or any drug candidates we may acquire or in-license, will obtain such orphan drug designation, pediatric exclusivity, new chemical entity exclusivity or any other market exclusivity in the United States, EU or any other territory, or that we will be the first to receive the respective regulatory approval for such drugs so as to be eligible for any market exclusivity protection.

Know-How

In addition to patents, we rely upon unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment provisions in the confidentiality agreements with our employees. These agreements are designed to protect our proprietary information and, in the case of the invention assignment provisions, to grant us ownership of technologies that are developed by our employees. These agreements may be breached, and we may not have adequate remedies for any breach.

To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

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 therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are usually not required to conduct, or submit results of, nonclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way 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.

The ANDA applicant is required to make certain certifications 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 label 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 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 from receiving the Paragraph IV certification, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant. Also, the ANDA 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 an active moiety that has not been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which time the FDA cannot accept any ANDA seeking approval of a generic version of that 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 for a generic drug that includes such changes.

An ANDA 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 may be filed before the expiration of the exclusivity period.

On August 23, 2018, Keryx submitted a Citizen Petition requesting, inter alia, that FDA recognize that Auryxia is eligible for five years of NCE exclusivity based on its novel active ingredient and for three years exclusivity for the IDA Indication. On January 19, 2019, FDA responded that Auryxia is eligible for a three-year exclusivity period for the IDA Indication, which expires on November 6, 2020. FDA, however, denied the NCE exclusivity based on its determination that Auryxia contains a previously-approved active moiety (ferric cation). FDA's decision on the Citizen Petition is subject to further review both within FDA and in the courts. On February 21, 2019, Akebia filed a Petition for Reconsideration of FDA's decision on the NCE determination for Auryxia.

Patent Term Extension

After NDA approval, owners of relevant drug patents or their agents may apply for up to a five-year patent extension for delays caused by FDA regulatory review. The allowable patent term extension is calculated as half of the drug's testing phase which is the time between IND submission and NDA submission, and all of the review phase, which is 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.

We have filed applications under the patent term extension provisions of 35 U.S.C. § 156 for U.S. Patent Nos. 8,299,298, 8,093,423, 7,767,851, 5,753,706, and 8,338,642 each of which covers Auryxia for delays caused by FDA regulatory review. If granted, we can utilize the patent term extension on one of these patents, however, we cannot assure you that we can obtain any extension of the term of these patents. Upon expiration of these patents, competitors who obtain the requisite regulatory approval may potentially offer products with the same composition and/or method of use as our product, so long as the competitors do not infringe any other patents that we may own or license.

For patents that might expire before a determination regarding patent term extension, the patent owner or its agent may request an interim patent term 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. We have filed for and received interim patent term extension in accordance with 35 U.S.C. § 156(e)(2) for U.S. Patent No. 5,753,706, which currently has an expiration date of February 3, 2020.

In addition, certain jurisdictions outside of the U.S., including Japan, have provisions that provide for patent term extension. In October 2014, following the regulatory approval of Riona in Japan, the Japan Patent office granted the patent term extensions filed by our sublicensee, JT, for Japanese Patents Nos. 4964585 and 4173553. As a result of the extension of patent term, Japanese Patents Nos. 4964585 and 4173553 will expire in November 2025 and November 2022, respectively.

Third-Party Filings

We are aware of certain United States patents issued to FibroGen, Inc., or FibroGen, directed to, among other things, purportedly new methods of using previously known heterocyclic carboxamide compounds for purposes of treating or affecting specified conditions. We do not believe these currently issued FibroGen United States patents will prevent us from commercializing vadadustat in the United States for the treatment of anemia due to CKD; nor do we make any admission that any of such patents are valid or enforceable. Under United States law, a person may be able to patent a discovery of a new way to use a previously known compound, even if such compound itself is patented, provided the newly discovered use is novel and non-obvious. Such a method-of-use patent, however, if valid, only protects the use of a claimed compound for the specified methods claimed in the patent. This type of patent does not prevent persons from using the compound for any previously known use of the compound. Further, this type of patent does not prevent persons from making and marketing the compound for an indication that is outside the scope of the patented method. We are not aware of any valid United States patents issued to FibroGen that claim methods of using any of our product candidates for purposes of inhibiting HIF-PHs for the treatment of anemia secondary to CKD.

We filed an opposition in Europe against FibroGen's European Patent No. 1463823, or the '823 EP Patent, and an oral proceeding took place March 8 and 9, 2016. Following the oral proceeding, the Opposition Division of the EPO ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen has appealed that decision and the appeal process is expected to take several years. Likewise, with regard to the invalidity proceeding that we filed in Japan against certain claims of FibroGen's Japanese Patent No. 4804131, or the '131 JP Patent, which is the Japanese counterpart to the '823 EP Patent, the Japan Patent Office, or JPO, issued a preliminary decision finding all of the challenged claims to be invalid. FibroGen subsequently amended the claims and the JPO accepted the amendments. The resulting '131 JP Patent does not cover vadadustat or any pyridine carboxamide compounds. To date, FibroGen has been unsuccessful in its attempts to obtain a patent in the United States covering the same claim scope as it obtained initially in Europe and Japan in the '823 EP Patent and '131 JP Patents. In the event FibroGen were to obtain such a patent in the United States, we may decide to challenge the patent as we have done in Europe and Japan.

On May 13, 2015, May 20, 2015 and July 6, 2015, we filed oppositions to FibroGen's European Patent Nos. 2322155, or the '155 EP Patent, 1633333, or the '333 EP Patent, and 2322153, or the '153 EP Patent requesting the patents be revoked in their entirety. These related patents claim, among other things, various compounds that either stabilize HIF or inhibit a HIF hydroxylase or a HIF prolyl hydroxylase for treating or preventing various conditions, including, inter alia, iron deficiency, microcytosis associated with iron deficiency, anemia of chronic disease, anemia wherein the subject has a transferrin saturation of less than 20%, anemia refractory to treatment with exogenously administered erythropoietin, or EPO, and microcytosis in microcytic anemia. Such method of use patents do not prevent persons from using the compound for other uses, including any previously known use of the compound. In particular, these patents do not claim methods of using any of our product candidates for purposes of inhibiting hypoxia-inducible factor prolyl hydroxylases, or HIF-PHs, for the treatment of anemia secondary to CKD. While we do not believe these patents will prevent us from commercializing vadadustat for the treatment of anemia secondary to CKD, we filed these oppositions to provide us and our collaborators with maximum flexibility for developing vadadustat and our pipeline of HIF-PH compounds.

Oppositions to the '155 EP Patent and the '153 EP Patent were also filed by Glaxo Group Limited, or Glaxo, and by Bayer Intellectual Property GmbH, Bayer Pharma Aktiengesellschaft, and Bayer Animal Health GmbH, or, collectively, Bayer.

With regards to the opposition that we filed in Europe against the ’333 EP Patent, an oral proceeding took place on December 8 and 9, 2016. Following the oral proceeding, the Opposition Division of the EPO ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. On December 9, 2016, FibroGen filed a notice to appeal the decision to revoke the ’333 EP Patent.

In oral proceedings held on May 29, 2017, regarding the ’155 EP Patent, the Opposition Division of the EPO ruled that the '155 EP Patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen filed a notice to appeal the decision to revoke the ’155 EP Patent on May 29, 2017.

Subsequently, in related oral proceedings held on May 31, 2017 and June 1, 2017 for the ’153 EP Patent, the Opposition Division of the EPO maintained the patent after FibroGen significantly narrowed the claims to an indication for which vadadustat is not intended to be developed. We and Glaxo separately filed notices to appeal the decision to maintain the ’153 EP Patent on November 9, 2017. Bayer filed a notice to appeal the decision on November 14, 2017.

Competition

The pharmaceutical and biotechnology industries are highly competitive. Our competitors include pharmaceutical companies and biotechnology companies, as well as universities and public and private research institutions. In addition, companies that are active in different but related fields represent substantial competition for us. Many of our competitors have significantly greater capital resources, larger research and development staffs and facilities and greater experience in drug development, regulation, manufacturing and marketing than we do. These organizations also compete with us to recruit qualified personnel, attract partners for joint ventures or other collaborations, and license technologies that are competitive with ours. To compete successfully in this industry, we must identify novel and unique drugs or methods of treatment and then complete the development of those drugs as treatments in advance of our competitors.

Auryxia

Hyperphosphatemia Competition

Auryxia is competing in the Hyperphosphatemia Indication in the United States with other FDA-approved phosphate binders such as Renagel® (sevelamer hydrochloride) and Renvela® (sevelamer carbonate), both marketed by Genzyme Corporation (a wholly-owned subsidiary of Sanofi), PhosLo® and Phoslyra® (calcium acetate), marketed by Fresenius Medical Care North America, Fosrenol® (lanthanum carbonate), marketed by Shire Pharmaceuticals Group plc, and Velphoro® (sucroferric oxyhydroxide), marketed by Fresenius Medical Care North America, as well as over-the-counter calcium carbonate products such as TUMS® and metal-based options such as aluminum, lanthanum and magnesium. Many of the phosphate binders listed above are now also available in generic forms. In addition, other phosphate binders are in development, including OPKO Health Inc.’s Alpharen™ tablets (fermagate tablets) and Ardelyx, Inc’s tenapanor, that may impact the market for Auryxia.

Iron Deficiency Anemia Competition

Auryxia is competing in the IDA Indication in the United States with over-the-counter oral iron, other prescription oral iron formulations, including ferrous gluconate, ferrous fumerate, and polysaccharide iron complex, and IV iron

formulations, including Feraheme® (ferumoxytol injection), Venofer® (iron sucrose injection), Ferrlicit® (sodium ferric gluconate complex in sucrose injection), Injectafer® (ferric carboxymaltose injection), and Triferic® (ferric pyrophosphate citrate).

In addition, other new therapies are in development for the treatment of IDA that may impact the market for Auryxia, such as Shield Therapeutics' Ferracrū® (ferric maltol), which is currently approved in Europe for IDA and is seeking FDA approval in the United States.

Vadadustat

If vadadustat is approved and launched commercially, competing branded drugs may include EPOGEN® (epoetin alfa) and Aranesp® (darbepoetin alfa), both commercialized by Amgen, Procrit® (epoetin alfa) and Eprex® (epoetin alfa), commercialized by Johnson & Johnson in the United States and Europe, respectively, and Mircera® (methoxy PEG-epoetin beta), commercialized by Vifor Pharma in the United States and Roche Holding Ltd. outside the United States. We may also face competition from potential new anemia therapies. There are several other HIF-PHI product candidates in various stages of active development for anemia indications that may be in direct competition with vadadustat if and when they are approved and launched commercially. These candidates are being developed by such companies as FibroGen, Japan Tobacco International, GlaxoSmithKline plc and Bayer HealthCare AG. FibroGen, together with its collaboration partners, Astellas Pharma Inc. and AstraZeneca PLC, is currently in global Phase 3 clinical

development of its product candidate, roxadustat. GlaxoSmithKline plc is currently in global Phase 3 clinical development of its product candidate, daprodustat. Japan Tobacco International and Bayer HealthCare AG are currently in Phase 3 clinical development of their product candidates in Japan. Some of these product candidates may launch in certain Asian markets as early as 2019. In addition, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce injectable ESA utilization and thus limit the market potential for vadadustat if they are approved and launched commercially. Other new therapies are in development for the treatment of conditions inclusive of renal anemia that may impact the market for anemia-targeted treatment.

A biosimilar is a biologic product that is approved based on demonstrating that it is highly similar to an existing, FDA-approved branded biologic product. The patents for the existing, branded biologic product must expire in a given market before biosimilars may enter that market without risk of being sued for patent infringement. In addition, an application for a biosimilar product cannot be approved by the FDA until 12 years after the existing, branded product was approved under a Biologics License Application, or BLA. The patents for epoetin alfa, an injectable ESA, expired in 2004 in the European Union, and the remaining patents expired between 2012 and 2016 in the United States. Because injectable ESAs are biologic products, the introduction of biosimilars into the injectable ESA market in the United States will constitute additional competition for vadadustat if we are able to obtain approval for and commercially launch our product. Several biosimilar versions of injectable ESAs are available for sale in the European Union. In the United States, Pfizer's biosimilar version of injectable ESAs, Retacrit® (epoetin alfa-epbx), was approved by the FDA in May 2018 and launched in November 2018 by Vifor Pharma.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sales, pricing, reimbursement, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory requirements, require the expenditure of substantial time and financial resources.

Review and Approval of Drug Products in the United States

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with applicable requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations and consistent with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, or ICH, requirements;

- submission to the FDA of an IND, which must be reviewed and active by the FDA before human clinical trials may begin;
- approval by an independent local or central institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed product candidate for each indication;
- preparation and submission to the FDA of a new drug application, or NDA, requesting marketing for one or more proposed indications;
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product candidate, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product candidate's identity, strength, quality and purity;

- satisfactory completion of FDA audits of clinical trial sites and records to assure compliance with GCPs and good practices, or GxPs, the integrity of the clinical data and that adequate controls and oversight are in place regarding manufacturing, clinical trials, pharmacovigilance, safety, data management, vendor oversight, collection and reporting of serious adverse events and other activities;
- payment of user fees and securing FDA approval of an NDA; and
- compliance with any post-approval requirements and/or commitments, including the potential requirement to implement a risk evaluation and mitigation strategy, or REMS, and potentially post-market requirement, or PMR, and commitment, or PMC, studies.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as in vitro and animal studies to assess the safety and activity of the product candidate for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, will likely continue after the IND is submitted through the time of the NDA submission.

The IND and IRB Processes

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their voluntary informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped through interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be obtained prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. As a required component of the IND application, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the submission of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold or require that the sponsor amend the clinical protocol to include additional safety measurements. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin (or resume if the clinical trial had been ongoing at the time a clinical hold was imposed).

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the

clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing, and controls, or CMC.

A sponsor may choose, but is not required, to conduct a foreign clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical trial is not conducted under an IND, the sponsor must ensure that the trial complies with certain FDA regulatory requirements in order to use the trial as support for an IND or application for marketing approval. These requirements to protect the rights, welfare, and safety of patients are also stipulated in applicable ICH guidance.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct a continuing review and reapprove the trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data monitoring committee, or DMC. DMCs may be charged with monitoring efficacy, safety, and/or study conduct. A DMC provides a recommendation for whether or not a clinical trial should move forward at designated check points based on available data from the trial. A recommendation by a DMC to suspend or terminate development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its website, https://clinicaltrials.gov/.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with initiation, conduct, or completion of clinical investigations that could support marketing approval of the product candidate or otherwise compromise the potential development of the product candidate.

On December 13, 2016, the 21st Century Cures Act, or Cures Act, established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies to make publicly

available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its product candidates available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in four sequential phases, which may overlap or be combined:

- Phase 1. The product candidate is initially introduced into a small number of healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition (e.g., cancer) and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- Phase 2. The product candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3. These clinical trials are commonly referred to as “pivotal” studies, which denote a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a product candidate. The product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product candidate for approval, identify adverse effects, establish the overall risk-benefit profile of the product candidate and to provide adequate information for the labeling of the product candidate.
- Phase 4. Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials conducted under the IND must be submitted at least annually to the FDA and, more frequently, if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA or the sponsor or the data monitoring committee may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB’s requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Under the Pediatric Research Equity Act of 2003, or PREA, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The legislation requires the FDA to meet with drug sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after the FDA’s receipt of the study plan. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

Submission of an NDA by the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things are submitted to the FDA as part of an NDA requesting approval to market the product candidate for one or more indications. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2019 is $2,588,478 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2019 is $309,915. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for product candidates with orphan designation and a waiver for certain small businesses.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. This is known as the filing decision. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to certain performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. A product that has been designated as a breakthrough therapy may also be eligible for review within six months if supported by clinical data at the time of submission of the NDA. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing such as active pharmaceutical ingredients, finished drug product manufacturing, control testing laboratories, as well as packaging and labeling facilities. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. The applicant of the NDA may also have their records, processes, procedures, training, and other aspects reviewed during an inspection. The FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain drug applications, including applications for drugs in a shortage or drugs for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks.

Finally, the FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track

application does not begin until the last section of the NDA is submitted. In addition, 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.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Improvement Act. This law established a new regulatory scheme allowing for expedited review of products designated as “breakthrough therapies.” A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's review clock goal for taking action on a marketing application from ten months to six months. For new chemical entities, or NCEs, the review clock starts after the NDA is filed with a total clock of twelve and eight months, respectively.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, analyses, or information in order for the FDA to reconsider the application. This may include the requirement to conduct another clinical study or studies. If and 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 such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements and Commitments

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, conditions of NDA approval may include sponsor agreement to PMR or PMC studies, which are designed to further assess drug safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. These may include additional studies, registries, data collection, analyses, and/or information.

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the

establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
    - product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a product candidate's safety or effectiveness are prohibited before the product candidate is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA or in a manner that is inconsistent with the product's prescribing information. In the United States, healthcare professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific conditions, for a manufacturer to engage in nonpromotional, truthful and non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. In addition, companies may also promote information that it consistent with the prescribing information and have the ability to proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug under some relatively recent guidance from the FDA. However, if a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products and drug samples are subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight months for a drug that has three or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of ''competitor generic therapies'' or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same

extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

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

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

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

Pediatric Studies and Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product is effective in the pediatric population studied, rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which an ANDA or 505(b)(2) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by the proposed product.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Drug Products Outside the United States

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Clinical Trial Approval in the European Union

Requirements for the conduct of clinical trials in the European Union including GCP are set forth in the Clinical Trials Directive 2001/20/EC, or the Clinical Trials Directive, and the GCP Directive 2005/28/EC, or the GCP Directive. Pursuant to the Clinical Trials Directive and the GCP Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the EU member states. Under this system, approval must be obtained from the competent national authority of each EU member state in which a study is planned to be conducted. To this end, a clinical trial application, or CTA, is submitted to the local competent authority in each country (or member state) where the clinical trial is being conducted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Clinical Trials Directive and the GCP Directive and other applicable guidance documents. These documents may be amended and/or updated by the EC at any time. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

In April 2014, the EU passed the new Clinical Trials Regulation (EU) No 536/2014, or the new Clinical Trials Regulation, which is set to replace the current Clinical Trials Directive. To ensure that the rules for clinical trials are identical throughout the European Union, the new EU clinical trials legislation was passed as a regulation that is directly applicable in all EU member states. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive until the new Clinical Trials Regulation becomes applicable. According to the current plans of the European Medicines Agency, or EMA, the new Clinical Trials Regulation is expected to become applicable in 2019. The Clinical Trials Directive will, however, still apply three years from the date of entry into application of the new Clinical Trials Regulation to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opts for old system.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trial in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the EU portal; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states; a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I is assessed jointly by all member states concerned, and Part II is assessed separately by each member state concerned); strictly defined deadlines for the assessment of clinical trial applications; and the involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Clinical Trials Regulation.

As in the United States, there are similar requirements in the European Union for posting clinical trial information online at the website, https://eudract.ema.europa.eu/, and in other countries as well.

PRIME Designation in the European Union

In March 2016, the EMA launched an initiative, the PRIority MEdicines, or PRIME, scheme, to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIME scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated agency contact and rapporteur from the Committee for Human Medicinal Products, or CHMP, or Committee for Advanced Therapies, or CAT, are appointed early in the PRIME scheme, facilitating increased understanding of the product at the EMA's committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Marketing Authorization

To obtain marketing approval of a product under EU regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a

centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various EU member states where such product has not received marketing approval in any EU member state before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Within this framework, manufacturers may seek approval of hybrid medicinal products under Article 10(3) of Directive 2001/83/EC. Hybrid applications rely, in part, on information and data from a reference product and new data from appropriate pre-clinical tests and clinical trials. Such applications are necessary when the proposed product does not meet the strict definition of a generic medicinal product, or bioavailability studies cannot be used to demonstrate bioequivalence, or there are changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration of the generic product compared to the reference medicinal product. In such cases the results of tests and trials must be consistent with the data content standards required in the Annex to the Directive 2001/83/EC, as amended by Directive 2003/63/EC.

Hybrid medicinal product applications have automatic access to the centralized procedure when the reference product was authorized for marketing via that procedure. Where the reference product was authorized via the decentralized procedure, a hybrid application may be accepted for consideration under the centralized procedure if the applicant shows that the medicinal product constitutes a significant therapeutic, scientific or technical innovation, or the granting of a community authorization for the medicinal product is in the interest of patients at the community level.

A marketing authorization may be granted only to an applicant established in the European Union. Regulation (EC) No. 1901/2006, or Pediatric Regulation, provides that prior to obtaining a marketing authorization in the European Union, an applicant must demonstrate compliance with all measures included in a Pediatric Investigation Plan, or PIP, approved by the Pediatric Committee of the EMA, or PDCO, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the marketing authorization is obtained in all member states of the European Union and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension. For orphan-designated medicinal products, the 10-year period of market exclusivity is extended to 12 years.

Periods of Authorization and Renewals in the European Union

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the relevant EU member state. To that end, the marketing authorization holder must provide the EMA or the relevant competent authority of the EU member state with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the relevant competent authority of the EU member state decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any marketing authorization that is not followed by the marketing of the medicinal product on the EU market (in the case of the centralized procedure) or on the market of the EU member state which delivered the marketing authorization within three years after authorization ceases to be valid.

Regulatory Data Exclusivity in the European Union

In the European Union, innovative medicinal products authorized in the European Union on the basis of a full marketing authorization application (as opposed to an application for marketing authorization that relies on data available in the marketing authorization dossier for another, previously approved, medicinal product) are entitled to eight years of data exclusivity. During this period, applicants for authorization of generics of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product. Innovative medicinal products are also entitled to ten years' market

exclusivity. During this ten-year period no generic of this medicinal product can be placed on the EU market. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Pediatric Studies and Exclusivity

Prior to obtaining a marketing authorization in the European Union, applicants must demonstrate compliance with all measures included in an EMA approved PIP covering all subsets of the pediatric population, unless the EMA has granted a product specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect the elderly population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP. If an applicant obtains a marketing authorization in all EU member states, or a marketing authorization granted in the Centralized Procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom (U.K.) voted in favor of leaving the European Union (commonly referred to as “Brexit”). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership of the European Union will automatically terminate two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on March 29, 2019 without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

Since the regulatory framework for pharmaceutical products in the U.K. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the U.K. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the U.K.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement 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 a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration, or Administration, have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services, or HHS, will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' advertisements to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D

plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. It is expected that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Outside the United States, ensuring adequate coverage and payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a clinical trial that compares the cost effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. 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 products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians, teaching hospitals and other healthcare providers, patient privacy laws and regulations, and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
-

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the U.S. Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- the federal transparency requirements, known as the federal Physician Payments Sunshine Act (renamed the Open Payments Act), under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- the PDMA and its implementation regulations, as well as the DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by third-party payors, including private insurers, and state gift ban and disclosure law requirements that differ from the federal Physician Payments Sunshine Act in terms of the nature and type of transfers of value that are reportable and the types of covered recipients.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, such as the Pharmaceutical Research and Manufacturers of America Code on Interactions with Health Care Professionals, known as the PhRMA Code. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare.

In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. The Affordable Care Act provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and will stay in effect through 2024 unless additional Congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, is no longer effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer

Americans to be insured by 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Congress will likely consider other legislation to replace elements of the ACA during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

Laws Relating to Foreign Trade

We are subject to various federal and foreign laws that govern our international business practices. These laws include the FCPA which prohibits U.S. companies and their representatives from paying, offering to pay, promising, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate for the purposes of obtaining or retaining business, or to otherwise obtain favorable treatment or influence a person working in an official capacity. In many countries, the health care professionals we regularly interact with may meet the FCPA's definition of a foreign government official. Additionally, interactions with or on the part of our partners, collaborators, contract research organizations, vendors or other agents may also implicate the FCPA. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect their transactions and to devise and maintain an adequate system of internal accounting controls. Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents unique challenges in the pharmaceutical industry because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments made by pharmaceutical companies to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Our international operations could also be subject to compliance with national laws of other countries, such as the United Kingdom Bribery Act. of 2010, or U.K. Bribery Act. The U.K. Bribery Act applies to any company "carrying on business" in the United Kingdom, irrespective of where the offending conduct occurs. The U.K. Bribery Act applies to bribery activities both in the public and private sector and prohibits the provision of an "advantage" intended to induce or reward "improper performance" of the recipient's function. The failure by a company to prevent third parties from providing a bribe on its behalf could also constitute an offense. Penalties under the U.K. Bribery Act include potentially unlimited fines for companies and criminal sanctions for corporate officers under certain circumstances.

There are local antibribery and anticorruption laws in countries where we are conducting clinical trials, such as Brazil and Russia, and many of these also carry the risk of significant financial or criminal penalties. Our clinical trial operations could also result in enforcement actions by U.S., U.K., or other governmental authorities. There are also trade laws within the United States and in other regions that regulate the sale, purchase, import, export, reexport, transfer and shipment of goods, currency, products, materials, services and technology. Violations of these laws can lead to serious consequences, including substantial fines.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Employees

As of December 31, 2018, we had 325 employees, 324 of whom were full-time. None of our employees is represented by any collective bargaining unit. We believe that we maintain good relations with our employees.

Available Information

Our principal executive offices are located at 245 First Street, Cambridge, Massachusetts 02142. Our telephone number is (617) 871-2098. Our website address is www.akebia.com. The information on our website or that may be accessed by links on our website is not incorporated by reference into this Form 10-K. We make available, free of charge and through our website, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and any amendments to any such reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after they are electronically filed with or furnished to the U.S. Securities and Exchange Commission.

Item 1A. Risk Factors

We face a variety of risks and uncertainties in our business. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also become important factors that affect our business. If any of the following risks occurs, our business, financial statements and future growth prospects could be materially and adversely affected.

Risks Related to our Merger with Keryx

We may fail to realize the anticipated benefits of our merger with Keryx, those benefits may take longer to realize than expected, and we may encounter significant integration difficulties and liabilities, which may have a material adverse effect on our business and financial position.

On December 12, 2018, we completed a merger, or the Merger, whereby Keryx Biopharmaceuticals, Inc., or Keryx, became a wholly owned subsidiary of ours. There can be no assurance that we will realize the full benefit of the anticipated synergies and cost savings relating to the Merger or that these benefits will be realized within the expected time frames or at all. Our ability to realize the anticipated benefits of the Merger will depend, to a large extent, on our ability to continue to integrate our business and Keryx's business and realize anticipated growth opportunities and synergies. If we are unable to successfully integrate the businesses, or integrate them in a timely fashion, we may face material adverse effects including, but not limited to (i) diversion of the attention of management and key personnel and potential disruption of our ongoing business, (ii) the loss of employees, (iii) challenges of managing a larger company, including challenges of conforming standards, controls, procedures and accounting and other policies and compensation structures, (iv) difficulties in achieving anticipated cost savings, (v) declines in our results of operations, financial condition or cash flows, (vi) a decline in the market price of our common stock, and (vii) potential liabilities, adverse consequences, increased expenses or other problems associated with our company following completion of the Merger. Many of these factors are outside of our control, and any one of them could result in increased costs, decreased expected revenues and further diversion of management time and energy, which could materially impact our business, financial statements and prospects.

In addition, following the Merger, we have become responsible for Keryx's liabilities and obligations, including with respect to legal, financial, regulatory and compliance matters, including certain post-approval regulatory requirements with respect to Auryxia and Fexeric, and obligations under collaboration, license, supply and manufacturing agreements. These obligations will result in additional cost and investment by us and, if we have underestimated the amount of these costs and investments or if we fail to satisfy any such obligations, we may not realize the anticipated benefits of the transaction. Also, due to the Merger and ongoing integration, we may forego or delay pursuit of other opportunities that may have proven to have greater commercial potential.

Further, it is possible that there may be unknown, contingent or other liabilities or problems that may arise in the future, the existence and/or magnitude of which we were previously unaware. Any such liabilities or problems could have an adverse effect on our business, financial condition or results of operations.

Lawsuits have been filed challenging the Merger and additional lawsuits may be filed in the future. Any rescission, monetary damages, or other adverse judgment could have a material adverse effect on us.

In October and November 2018, four purported shareholders of Keryx filed four separate putative class actions against Keryx and the former members of Keryx's Board of Directors and, with respect to one action, Alpha Therapeutics Merger Sub, Inc. and Akebia, challenging the disclosures made in connection with the Merger. Among other things, the complaints seek rescission of the Merger or rescissory damages; a declaration that that the defendants violated Sections 14(a) and 20(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and Rule 14a-9 thereunder; and an award of plaintiffs' costs, including reasonable allowance for attorneys' fees and experts' fees. In

addition, in December 2018, a purported stockholder of Keryx filed a complaint against Keryx pursuant to Section 220 of the Delaware General Corporation Law, which seeks inspection of various Keryx books and records, purportedly to investigate "possible wrongdoing," in connection with Keryx's negotiation and approval of the Merger, as well as the independence of former members of Keryx's Board of Directors (some of whom are current members of our Board of Directors). In addition to the production of books and records, the Section 220 action seeks costs and expenses incurred in the action, including reasonable attorneys' fees. See Part I, Item 3. Legal Proceedings for further information relating to the lawsuits. Additional lawsuits arising out of the Merger may be filed in the future. We could be forced to expend significant resources in the defense of these lawsuits, including but not limited to, costs associated with the indemnification of Keryx and Akebia directors and officers, and the lawsuits, regardless of outcome, could have a negative effect on our reputation, stock price and results of operations. In addition, rescission of the Merger, monetary damages or other adverse judgment would have a material adverse effect on our business and financial position.

Our financial statements include goodwill and other intangible assets as a result of the Merger. These assets could become impaired in the future under certain conditions.

Accounting standards in the United States require that one party to the Merger be identified as the acquirer. In accordance with these standards, the Merger was accounted for as an acquisition of all outstanding shares of Keryx common stock by us, as the acquirer, and followed the acquisition method of accounting for business combinations. Our assets and liabilities were consolidated with those of Keryx on our financial statements. We measured Keryx's assets acquired and liabilities assumed by us at their fair values, including net tangible and identifiable intangible assets acquired and liabilities assumed, as of the consummation of the Merger. The excess of the purchase price over the fair value of Keryx's assets and liabilities was recorded as goodwill. The Merger added approximately $384.7 million of goodwill and definite lived intangible assets to our financial statements. In accordance with generally accepted accounting principles, or GAAP, we will be required at least annually to review the carrying value of our goodwill, and for definite lived intangible assets when indicators of impairment are present, to determine if any adverse conditions exist or a change in circumstances has occurred that would indicate impairment of the value of these assets. Conditions that could indicate impairment and necessitate an evaluation of these assets include, but are not limited to, a significant adverse change in the business climate or the legal or regulatory environment within which we operate. In addition, the deterioration of a company's market capitalization significantly below its net book value is an indicator of impairment. To the extent goodwill or other intangible assets become impaired, we may be required to incur material charges relating to such impairment. Such a potential impairment charge could have a material impact on our future operating results and financial position.

Risks Related to our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception, and anticipate that we will continue to incur significant losses and cannot guarantee when, if ever, we will become profitable or attain positive cash flows.

Investment in pharmaceutical product development and commercialization is highly speculative because it entails upfront capital expenditures and significant risk that a product candidate will fail to gain marketing approval or that an approved product will not be commercially viable. Since our inception, we have devoted most of our resources to research and development, including our preclinical and clinical development activities and, following the Merger, commercialization. We have financed our operations primarily through sales of equity securities, our strategic collaborations and, following the Merger, product revenues. Prior to the Merger, we had no products approved for commercial sale and had not generated any revenue from the sale of products. We are not currently profitable and have incurred net losses each year since our inception, including net losses of $143.6 million for the year ended December 31, 2018. As of December 31, 2018, we had an accumulated deficit of $514.4 million. We cannot guarantee when, if ever, we will become profitable. Our ability to generate product revenue and achieve profitability depends significantly on our success in many areas, including the following:

- developing, commercializing and marketing Auryxia, vadadustat, if approved, or any other product or product candidate, including those that may be in-licensed or acquired;
- completing preclinical and clinical development of our product candidates;
- seeking and obtaining marketing approvals for our product candidates after completion of clinical studies and the timing of such approvals;
- developing sustainable and scalable manufacturing processes for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate products that are compliant with good manufacturing practices, or GMPs, and services to support the clinical development and the market demand for our products and product candidates, including those that may be in-licensed or acquired;

- launching and commercializing our product candidates, either directly or with a collaborator or distributor;
- obtaining sufficient pricing and reimbursement for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired from private and governmental payors;
- obtaining market acceptance of Auryxia, vadadustat and any other product candidate, including those that may be in-licensed or acquired as viable treatment options;
- the size of any market in which Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, receive approval and obtaining adequate market share in those markets;

- addressing any competing products;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any transaction into which we may enter, including collaboration, merger, acquisition and licensing arrangements;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. The amount of our future net losses will depend, in part, on the rate of our future expenditures, and our financial position will depend, in part, on our product revenues and our ability to obtain funding through equity or debt financings or strategic collaborations. We expect to continue to incur significant expenses if and as we:

- conduct our development program of vadadustat for the treatment of anemia due to chronic kidney disease, or CKD, including $PRO_2TECT$, $INNO_2VATE$, $FO_2RWARD$-2, $TRILO_2GY$-2 and $EXPLO_2RE$, and develop plans for and conduct the preclinical and clinical development of any other potential product candidates;
- continue our commercialization activities for Auryxia and plan for the commercialization of vadadustat, if approved, and any other product candidate;
    - continue our Merger-related integration activities;
- seek marketing approvals for our product candidates that successfully complete clinical studies, and maintain marketing approvals for Auryxia and any product candidate for which we obtain marketing approval, including complying with any post-marketing regulatory requirements;
- have our product candidates manufactured for clinical trials and for commercial sale;
- initiate additional preclinical, clinical or other studies for vadadustat and any other product candidates, or any post-marketing approval studies, Phase 4 studies or any other clinical trials for Auryxia and Fexeric;
- seek to discover and develop additional product candidates;
- engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we would market and develop commercial products, or develop other product candidates and technologies;
- make royalty, milestone or other payments under our license agreements and any future in-license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel;
- continue to create additional infrastructure and expend additional resources to support our operations as a public company, including any additional infrastructure and resources necessary to support a transition from our status as an emerging growth company; and
- experience any delays or encounter issues with any of the above.

We also could be forced to expend significant resources in the defense of the pending securities class action and shareholder derivative lawsuits brought against us, Keryx and certain of Keryx's former directors and officers, some of whom are current directors and officers of ours, and other legal proceedings, as described under Part I, Item 3. Legal Proceedings, or any other such lawsuits brought against us in the future.

Because of the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of increased expenses. The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter, the progress of our clinical development and our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

Even if we succeed in receiving marketing approval for and are able to commercialize vadadustat, we will continue to incur substantial research and development and other expenditures to develop and market, if approved, any other product candidates as well as any costs relating to post-marketing requirements for Auryxia, vadadustat and any other product candidates that may receive marketing approval. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory authorities, or if we otherwise believe it is necessary, to change our manufacturing processes or assays, to amend or replace our study protocols, to repeat any of our clinical trials, to perform studies in addition to, different from or larger than those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates. Even if our product candidates are approved for commercial sale, we anticipate incurring significant costs associated with commercializing Auryxia, vadadustat, if approved, and any other approved product candidate. In addition, our ability to generate revenue would be negatively affected if the size of our addressable patient population is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the patient population for treatment is narrowed by competition, physician choice, coverage or reimbursement, or payor or treatment guidelines. Even though we generate revenue from Auryxia and may generate revenues from the sale of any product candidates that may be approved in the future, we may never generate revenue that is significant enough to become and remain profitable, and we may need to obtain additional funding to continue operations.

We will require substantial additional financing to achieve our goals. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.

As of December 31, 2018, our cash and cash equivalents and available for sale securities were $321.6 million. We expect to continue to expend substantial amounts for the foreseeable future continuing to commercialize Auryxia and developing and commercializing vadadustat, if approved, and any other product candidates. These expenditures will include costs associated with research and development, potentially obtaining marketing approvals and having our products manufactured, as well as marketing and selling products approved for sale, if any. In addition, other unanticipated costs may arise, including as a result of our decision to include certain elements in our development programs. Because the outcome of our current and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amount of funding necessary to successfully complete the development and commercialization of our product candidates. Our future capital requirements depend on many factors, including:

- significant costs associated with our global Phase 3 development program for vadadustat for the treatment of anemia due to CKD. As of December 31, 2018, we expect the remaining external aggregate contract research organization, or CRO, costs of $PRO_2TECT$ and $INNO_2VATE$, which are designed to enroll up to approximately 7,600 subjects, to be in the range of $190.0 million to $220.0 million; the estimated costs for $PRO_2TECT$ and $INNO_2VATE$ could increase significantly due to a number of factors, including changes in target enrollment and enrollment rates, accrual of major adverse cardiovascular events, or MACE, detection of unexpected safety signals, the addition of new investigative sites, modification of clinical trial protocols, performing other studies in support of the Phase 3 program, choosing to add third-party vendors to support the program, and any other factor that could delay completion of $PRO_2TECT$ and $INNO_2VATE$;
- the cost and timing of commercialization activities for Auryxia and our product candidates, if approved for marketing, including product manufacturing, marketing, sales and distribution costs;
- the results of our meetings with the FDA, the EMA and other regulatory authorities and any consequential effects on study design, study size and resulting operating costs;
- difficulties or delays in enrolling patients in our clinical trials;
- the timing of, and the costs involved in, obtaining marketing approvals for vadadustat and any other product candidates that we may develop or acquire, including to fund the preparation and filing of regulatory submissions

with the FDA, the EMA and other regulatory authorities, if clinical studies are successful;

- the cost of conducting the $FO_2$RWARD-2, TRIL$O_2$GY-2 and EXPL$O_2$RE clinical studies or any post-marketing approval studies, Phase 4 studies or any other clinical trials for Auryxia and Fexeric;
- the cost, timing and outcome of our efforts to obtain marketing approval for vadadustat in the United States, Europe and in other jurisdictions;
- the scope, progress, results and costs of additional preclinical, clinical, or other studies for vadadustat and Auryxia, as well as any studies of any other product candidates;

- the cost of securing and validating commercial manufacturing of vadadustat and maintaining our manufacturing arrangements for Auryxia, or securing and validating additional arrangements;
- the costs involved in preparing, filing and prosecuting patent applications and maintaining, defending and enforcing our intellectual property rights, including litigation costs, and the outcome of such litigation;
- the costs involved in any legal proceedings to which we are a party;
- Merger-related integration costs;
- our ability to attract, hire and retain qualified personnel; and
- the extent to which we engage in transactions, including collaboration, merger, acquisition and licensing transactions pursuant to which we would develop and market commercial products, or develop other product candidates and technologies.

Furthermore, we expect to continue to incur additional costs associated with operating as a public company, including any additional infrastructure and resources necessary to support a transition from our status as an emerging growth company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We expect our cash resources, including the timing of committed research and development funding from our collaborators, to fund our current operating plan into the third quarter of 2020. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Furthermore, our development milestones may not be achieved, we may not receive the anticipated funding from our collaboration partners, and we may not secure other sources of financing. If and until we can generate a sufficient amount of product revenues, we expect to finance future cash needs through public or private equity or debt offerings, payments from our collaborators, strategic transactions, or a combination of these approaches. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic objectives.

We also have a $40.0 million revolving loan facility, or the Revolving Loan Facility, with Silicon Valley Bank, or SVB. The borrowing base under the Revolving Loan Facility, or any other asset-based credit facility into which we may enter in the future, may be significantly lower than the total commitment under any such facility and therefore may limit the total amount we may be able to borrow. As of December 31, 2018, we had approximately $16.0 million in available borrowing base under the Revolving Loan Facility, of which $15.0 million had been drawn down. In addition, the Revolving Loan Facility includes certain restrictive covenants, including the requirement to maintain compliance with a liquidity ratio. Upon an event of default under the Revolving Loan Facility, SVB is entitled to accelerate and demand payment of all amounts outstanding under Revolving Loan Facility, stop advancing money or extending credit to Keryx, demand that Keryx deposit at least 105% of the face amount of any letters of credit remaining undrawn to secure all obligations thereunder, and exercise other remedies available to SVB under the Revolving Loan Facility and at law or in equity. We have determined that events of default have already occurred, and we have not obtained a formal waiver from SVB with respect to these events of default. As a result, we have classified the outstanding principal of $15.0 million as a current liability in our consolidated balance sheet as of December 31, 2018. So long as these events of default are not waived or otherwise resolved, SVB has the right to take any of the foregoing remedies. If SVB were to accelerate all of the obligations outstanding under the Revolving Loan Facility, we would be required to pay the outstanding principal and other fees to SVB, and we would no longer have access to the Revolving Loan Facility. We expect our cash resources to fund our current operating plan into the third quarter of 2020, which assumes the payment of all amounts due to SVB and no future borrowings under the Revolving Loan Facility. We cannot assure that we will be able to obtain alternative sources of financing on favorable terms or at all.

Any additional fundraising efforts may divert our management’s attention away from their day-to-day activities, which may adversely affect our ability to develop and commercialize Auryxia, vadadustat and any other product candidates. Also, additional funds may not be available to us in sufficient amounts or on acceptable terms or at all. If we are

unable to raise additional capital in sufficient amounts when needed or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of Auryxia, vadadustat and any other product candidates. Any of these events could significantly harm our business, financial condition and prospects.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product and product candidates on unfavorable terms to us.

We expect to finance our cash needs through product revenues, public or private equity or debt offerings, payments from our collaborators, strategic transactions, or a combination of these approaches. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, our fixed payment obligations may increase, any such securities may have rights senior to those of our common stock, and the terms may include liquidation or other preferences and anti-dilution protections that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, make capital expenditures, declare dividends, acquire, sell or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic transactions with third parties, we may have to do so at an earlier stage than otherwise would be desirable. In connection with any such strategic transactions, we may be required to relinquish valuable rights to our product and product candidates, future revenue streams or research programs or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts for Auryxia, vadadustat, or any other product candidates that we develop or acquire, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We may engage in strategic transactions to acquire assets, businesses, or rights to products, product candidates or technologies or form collaborations or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, increase our debt, or cause us to incur significant expense.

As part of our business strategy, we may engage in additional strategic transactions to expand and diversify our portfolio, including through the acquisition of assets, businesses, or rights to products, product candidates or technologies or through strategic alliances or collaborations, similar to the Merger and our collaboration and license arrangements. We may not identify suitable strategic transactions, or complete such transactions in a timely manner, on a cost-effective basis, or at all. Moreover, we may devote resources to potential opportunities that are never completed or we may incorrectly judge the value or worth of such opportunities. Even if we successfully execute a strategic transaction, we may not be able to realize the anticipated benefits of such transaction, may incur additional debt or assume unknown or contingent liabilities in connection therewith, and may experience losses related to our investments in such transactions. Integration of an acquired company or assets into our existing business may not be successful and may disrupt ongoing operations, require the hiring of additional personnel and the implementation of additional internal systems and infrastructure, and require management resources that would otherwise focus on developing our existing business. Even if we are able to achieve the long-term benefits of a strategic transaction, our expenses and short-term costs may increase materially and adversely affect our liquidity. Any of the foregoing could have a detrimental effect on our business, results of operations and financial condition.

In addition, future transactions may entail numerous operational, financial and legal risks, including:

- incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- exposure to known and unknown liabilities, including possible intellectual property infringement claims, violations of laws, tax liabilities and commercial disputes;
- higher than expected acquisition and integration costs;
- difficulty in integrating operations and personnel of any acquired business;
- increased amortization expenses or, in the event that we write-down the value of acquired assets, impairment losses;
- impairment of relationships with key suppliers or customers of any acquired business due to changes in management and ownership;

- inability to retain personnel, customers, distributors, vendors and other business partners integral to an in-licensed or acquired product, product candidate or technology;
- potential failure of the due diligence processes to identify significant problems, liabilities or other shortcomings or challenges;
- entry into indications or markets in which we have no or limited direct prior development or commercial experience and where competitors in such markets have stronger market positions; and
- other challenges associated with managing an increasingly diversified business.

If we are unable to successfully manage any transaction in which we may engage, our ability to develop new products and continue to expand and diversify our portfolio may be limited.

Risks Related to Commercialization

Our ability to successfully commercialize our product, Auryxia, our late-stage product candidate, vadadustat, if approved, and any other product or product candidate, including our ability to achieve their widespread market acceptance, is critical to the success of our business.

Our ability to generate significant product revenue will depend almost entirely on our ability to execute on our commercialization plans and the level of market adoption for, and the continued use of, our product, Auryxia, and, if approved, our late-stage product candidate, vadadustat, by physicians, hospitals, patients, and/or healthcare payors, including government payors, consumers, managed care organizations and specialty pharmacies. If we are not successful in commercializing Auryxia and vadadustat, if approved, including achieving and maintaining an adequate level of market adoption, our profitability and our future business prospects will be adversely impacted. Market acceptance of Auryxia and any other product candidate that may be approved, including vadadustat depends on a number of other factors, including:

- the availability of adequate coverage and reimbursement by third-party payors and governmental authorities;
- the safety and efficacy of the product, as demonstrated in clinical trials and in the post-marketing setting;
- the prevalence of the disease treated by our product;
- the clinical indications for which the product is approved and the product label approved by regulatory authorities, including any warnings or limitations that may be required on the label as a consequence of potential safety risks associated with the product;
- the countries in which marketing approvals are obtained;
- the claims we and our collaborators are able to make regarding the safety and efficacy of our products;
- the success of our physician and patient communications and education programs;
- acceptance by physicians and patients of the product as a safe and effective treatment and the willingness of the target patient population to try new therapies and of physicians to prescribe new therapies;
- the cost, safety and efficacy of the product in relation to alternative treatments;
- the timing of receipt of marketing approvals and product launch relative to competing products and potential generic entrants;
- relative convenience and ease of administration;
- the prevalence and severity of adverse side effects;
- adverse publicity about our products or favorable or adverse publicity about competing products;
- the effectiveness of our and our collaborators' sales, marketing and distribution efforts; and
- the restrictions on the use of our products together with other medications, if any.

Market acceptance is critical to our ability to generate significant product revenue. In addition, any product or product candidate, if approved and commercialized, may achieve only limited market acceptance or none at all. If any of our approved products is not accepted by the market to the extent that we expect, we may not be able to generate product revenue and our business would suffer.

Generic competitors are seeking approval of generic versions of Auryxia and the market entry of one or more generic competitors would limit Auryxia sales and have an adverse impact on our business and results of operation.

Although composition and use of Auryxia are currently claimed by 14 issued patents that are listed in the FDA's Orange Book, we cannot assure you that we will be successful in defending against third parties attempting to invalidate or design around our patents or assert that our patents are invalid or otherwise unenforceable or not infringed, or in competing against third parties introducing generic equivalents of Auryxia or any of our future

products.

The Hatch-Waxman Act allows applicants seeking to market a generic equivalent of a drug product that relies, in whole or in part, on the FDA's prior approval of a patented brand name drug, to provide notice to the holder of the New Drug Application for the brand name drug of its application, called a Paragraph IV certification notice, if the applicant is seeking to market its product prior to the expiration of the patents with claims directed to the brand name drug. After the introduction of a generic competitor, a significant percentage of the prescriptions written for a product may be filled with the generic version, resulting in a loss in sales of the branded product. To date, we have received four Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the FDA requesting approval for generic versions of Auryxia tablets (210 mg iron per tablet). For more information on these Paragraph IV certification notice letters and any related litigation, see Part I, Item 3. Legal Proceedings. Generic competition for Auryxia or any of our future products could have a material adverse effect on our sales, results of operations and financial condition.

In addition, litigation to enforce or defend intellectual property rights is complex, costly and involves significant management time. If our Orange Book listed patents are successfully challenged by a third party and a generic version of Auryxia is approved and launched, revenue from Auryxia could decline significantly which would have a material adverse effect on our sales, results of operations and financial condition.

If we are unable to maintain sales, marketing and distribution capabilities or to enter into additional agreements with third parties, we may not be successful in commercializing Auryxia or any of our product candidates if they are approved.

In order to market Auryxia, we intend to continue to invest in sales and marketing, which will require substantial effort and significant management and financial resources. We will need to devote significant effort, in particular, to recruiting individuals with experience in the sales and marketing of pharmaceutical products. Competition for personnel with these skills is significant.

There are risks involved with maintaining our own sales, marketing and distribution capabilities, including the following:

- potential inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- potential inability of sales personnel to obtain access to physicians;
- potential lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- costs and expenses associated with maintaining our own sales and marketing organization.

If we are unable to maintain our own sales, marketing and distribution capabilities and our arrangements with third parties with respect to sales, marketing and distribution, or we are unsuccessful in entering into additional arrangements with third parties to sell, market and distribute our product candidates or are unable to do so on terms that are favorable to us, we will not be successful in commercializing our product candidates.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product and product candidates, if approved, which could make it difficult for us to sell any approved products profitably.

Market acceptance and sales of any approved products will depend significantly on the availability of adequate coverage and reimbursement from third-party payors and may be affected by existing and future healthcare reform measures. Government authorities and third-party payors decide which drugs they will cover, as well as establish formularies or implement other mechanisms to manage utilization of products and determine reimbursement levels. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient; and
- cost effective.

49

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor. In the United States, there are multiple government and private third-party payors with varying coverage and reimbursement levels for pharmaceutical products. Within Medicare, for oral drugs dispensed by pharmacies and also administered in facilities, coverage and reimbursement may vary depending on the setting. The Centers for Medicare & Medicaid Services, or CMS, local Medicare administrative contractors and/or Medicare Part D plans may have some responsibility for determining the medical necessity of such drugs, and therefore coverage, for different patients. Different reimbursement methodologies may apply, and CMS may have some discretion in interpreting their application in certain settings. As an oral drug, Auryxia is covered by Medicare only under Part D. In September 2018, CMS communicated to Medicare Part D sponsors that CMS does not consider Auryxia to be covered under Part D when it is used solely for the treatment of iron deficiency anemia in patients with CKD not on dialysis, or the IDA Indication. CMS does, however, consider Auryxia to be a covered Part D drug when it is used for its other FDA-approved indication: the control of serum phosphorus levels in CKD patients on dialysis, or the Hyperphosphatemia Indication. As a result, Part D sponsors now utilize a prior authorization edit or other process for all Auryxia prescriptions for Medicare beneficiaries to ensure that Auryxia is being used for the Part D covered indication. We are engaging in discussions with CMS and Part D sponsors on this matter as we believe that Auryxia should qualify for coverage under Part D of the CMS regulations when it is used for the IDA Indication. If we are unsuccessful in our efforts to obtain Part D coverage for the IDA Indication, our ability to commercialize Auryxia for this indication will be adversely impacted. While we believe that the vast majority of the Part D prescriptions written for Auryxia today are for the Hyperphosphatemia Indication and therefore will continue to be covered by Part D plans with prior authorization, the prior authorization requirement may have an adverse impact on market acceptance of Auryxia and may influence physicians' prescribing decisions. We cannot predict the impact of the CMS determination or prior authorization changes on our operations and they could have a material adverse effect on our revenue and results of operations going forward.

Medicaid reimbursement of drugs will also vary by state. Private third-party payor reimbursement policies may also vary and may or may not be consistent with Medicare reimbursement methodologies. Manufacturers of outpatient prescription drugs may be required to provide discounts or rebates under government healthcare programs or to certain third-party payors in order to obtain coverage of such products.

Additionally, we may be required to enter into contracts with third-party payors offering rebates or discounts on our products in order to obtain favorable formulary status. We may not be able to agree upon commercially reasonable terms with such third-party payors or provide data sufficient to obtain favorable coverage and reimbursement for many reasons, including that we may be at a competitive disadvantage relative to companies with more extensive product lines. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Even if we obtain coverage for any approved product, third-party payors may not establish adequate reimbursement amounts which may reduce the demand for our product and prompt us to have to reduce pricing for the products. If reimbursement is not available or is limited, we may not be able to commercialize certain of our products. In addition, in the United States third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and reimbursement levels for new drugs. As a result, significant uncertainty exists as to whether and how much reimbursement third-party payors will provide for newly approved drugs which, in turn, will put downward pressure on the pricing of drugs.

If vadadustat is approved and included in the fixed reimbursement model for a bundle of dialysis services, or the bundle, we would be required to enter into contracts to supply vadadustat to specific dialysis clinics, instead of through third-party payors, which we believe could be challenging. In May 2017, we entered into a license agreement pursuant to which we will grant Vifor (International) Ltd., or Vifor Pharma, an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, in the United States, subject to FDA approval and inclusion in the bundle. Under this license agreement with Vifor Pharma, or the Vifor Agreement, FKC is not obligated to utilize

vadadustat in its clinics. In addition, even if FKC chooses to utilize vadadustat in its clinics in the United States, it is not restricted from utilizing other therapies for anemia due to CKD. The Vifor Agreement does not restrict us from entering into supply agreements with other dialysis clinics, such as DaVita, one of the largest operators of dialysis clinical in the United States, however, the dialysis clinics may choose not to contract with us for vadadustat or they may choose to contract with us for a limited supply of vadadustat. Although we currently believe it is likely that vadadustat will be included in the bundle, if vadadustat is not included in the bundle, then the Vifor Agreement will not become effective, and patients would access vadadustat through contracts we negotiate with third-party payors for reimbursement of vadadustat, which would be subject to the risks and uncertainties described above. Additionally, if there are updates to the recently published Transitional Drug Add-On Payment Adjustment, or TDAPA, rule that decreases the basis for reimbursement during the transition period or if TDAPA is eliminated, then our profitability may be adversely affected. We may be unable to sell vadadustat, if approved, to dialysis providers on a profitable basis if CMS significantly reduces the level of reimbursement for dialysis services and providers choose to use alternative therapies or look to negotiate their contracts with us. Our profitability may also be affected if our costs of production increase faster than increases in reimbursement levels. Adequate coverage and reimbursement of our products by government and private insurance plans is central to patient and provider acceptance of any products for which we receive marketing approval.

Price controls may be imposed, which may adversely affect our future profitability.

In some countries, including member states of the European Union, or EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take a significant amount of time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices, and in certain instances render commercialization in certain markets infeasible or disadvantageous from a financial perspective. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or government authorities may lead to further pressure on the prices or reimbursement levels. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, the commercial launch of our product candidate could be delayed, possibly for lengthy periods of time, we or our collaborators may not launch at all in a particular country, we may not be able to recoup our investment in one or more product candidates, and there could be a material adverse effect on our business.

Recently, there has been considerable public and government scrutiny in the United States of pharmaceutical pricing and proposals to address the perceived high cost of pharmaceuticals. There have also been several recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices or price increases. Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our product candidates, if approved, and could diminish our ability to establish what we believe is a fair price for our products, ultimately diminishing our revenue for our products if they are approved.

Approval of Fexeric in the EU does not ensure successful commercialization and reimbursement.

On September 23, 2015, the European Commission, or EC, approved Fexeric for the control of elevated serum phosphorus levels, or hyperphosphatemia, in adult patients with CKD, including pre-dialysis and dialysis patients. The EC also considered ferric citrate coordination complex as a New Active Substance, or NAS, which provides 10 years of data and marketing exclusivity in the EU.

Fexeric has never been marketed in the EU, and we do not intend to commercialize Fexeric in the EU on our own. We have not been successful in finding a suitable commercialization partner for Fexeric in the EU to date. We cannot assure you that we will be able to find a suitable commercialization partner in the EU or otherwise create value from our European rights. The EC’s approval of Fexeric in the EU was contingent on, among other things, our commencing marketing of Fexeric by September 23, 2018, however, we received an extension to March 25, 2019, and a subsequent extension to December 23, 2019. If we are unable to commence marketing Fexeric in the EU by December 23, 2019, the Fexeric approval in the EU will cease to be valid. We are working with Panion & BF Biotech, Inc., or Panion, the licensor of our rights to ferric citrate to formulate a commercial plan for Fexeric in Europe. See below for additional information about our arrangements with Panion. There can be no assurances that we will successfully work with Panion with respect to the European commercialization of Fexeric in a timely manner or at all, or that the EC will not

revoke its approval of Fexeric if we fail to market Fexeric by the deadline or for any other reason.

The commercial success of Fexeric is subject to the same types of risks we face with commercializing Auryxia in the United States. In addition, in European countries, pricing and payment of prescription pharmaceuticals is subject to more extensive governmental control than in the United States. Pricing negotiations with European governmental authorities can take six to twelve months or longer after the receipt of regulatory approval and product launch. If reimbursement for Fexeric is unavailable in any country in which reimbursement is sought, limited in scope or amount, or if pricing is set at or reduced to unsatisfactory levels, our ability or any potential partner's ability to successfully commercialize Fexeric in such a country would be impacted negatively. Furthermore, if these measures prevent us or any potential partner from selling Fexeric on a profitable basis in a particular country, they could prevent the commercial launch or continued sale of Fexeric in that country. We may never commercialize Fexeric in the EU or reach or maintain profitability with respect to Fexeric in the EU.

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

The development and commercialization of new drugs is highly competitive and subject to rapid and significant technological change. Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the development and commercialization of our product and product candidates. Our objective is to continue to commercialize Auryxia and develop and commercialize new products with superior efficacy, convenience, tolerability and/or safety. In many cases, any approved products that we commercialize will compete with existing, market-leading products.

Auryxia is competing in the hyperphosphatemia market in the United States with other FDA-approved phosphate binders such as Renagel® (sevelamer hydrochloride) and Renvela® (sevelamer carbonate), both marketed by Genzyme Corporation (a wholly-owned subsidiary of Sanofi), PhosLo® and Phoslyra® (calcium acetate), marketed by Fresenius Medical Care North America, Fosrenol® (lanthanum carbonate), marketed by Shire Pharmaceuticals Group plc, and Velphoro® (sucroferric oxyhydroxide), marketed by Fresenius Medical Care North America, as well as over-the-counter calcium carbonate products such as TUMS® and metal-based options such as aluminum, lanthanum and magnesium. Many of the phosphate binders listed above are now also available in generic forms. In addition, other phosphate binders are in development, including OPKO Health Inc.'s Alpharen™ tablets (fermagate tablets) and Ardelyx, Inc.'s tenapanor, that may impact the market for Auryxia.

Auryxia is competing in the IDA market in the United States with over-the-counter oral iron, ferrous sulfate, other prescription oral iron formulations, including ferrous gluconate, ferrous fumerate, and polysaccharide iron complex, and IV iron formulations, including Feraheme® (ferumoxytol injection), Venofer® (iron sucrose injection), Ferrlicit® (sodium ferric gluconate complex in sucrose injection), Injectafer® (ferric carboxymaltose injection), and Triferic® (ferric pyrophosphate citrate).

In addition, other new therapies are in development for the treatment of IDA that may impact the market for Auryxia, such as Shield Therapeutics' Ferracru® (ferric maltol), which is currently approved in Europe for IDA and is seeking FDA approval in the United States.

Furthermore, Aurxyia's commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective or safer than Auryxia. Other companies have product candidates in various stages of pre-clinical or clinical development to treat diseases for which we are marketing Auryxia.

If vadadustat is approved and launched commercially, competing drugs may include EPOGEN® (epoetin alfa) and Aranesp® (darbepoetin alfa), both commercialized by Amgen, Procrit® (epoetin alfa) and Eprex® (epoetin alfa), commercialized by Johnson & Johnson in the United States and Europe, respectively, and Mircera® (methoxy PEG-epoetin beta), commercialized by Vifor Pharma in the United States and Roche Holding Ltd. outside the United States. We may also face competition from potential new anemia therapies. There are several other HIF-PHI product candidates in various stages of development for anemia indications that may be in direct competition with vadadustat if and when they are approved and launched commercially. These candidates are being developed by such companies as FibroGen, Japan Tobacco International, GlaxoSmithKline plc and Bayer HealthCare AG. FibroGen, together with its collaboration partners, Astellas Pharma Inc. and AstraZeneca PLC, is currently in global Phase 3 clinical development of its product candidate, roxadustat. GlaxoSmithKline plc is currently in global Phase 3 clinical development of its product candidate, daprodustat. Japan Tobacco International and Bayer HealthCare AG are currently in Phase 3 clinical development of their product candidates in Japan. Some of these product candidates may launch in certain Asian markets as early as 2019. In addition, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce injectable ESA utilization and thus limit the market potential for vadadustat if they are approved and launched commercially. Other new therapies are in development for

the treatment of conditions inclusive of renal anemia that may impact the market for anemia-targeted treatment.

A biosimilar is a biologic product that is approved based on demonstrating that it is highly similar to an existing, FDA-approved branded biologic product. The patents for the existing, branded biologic product must expire in a given market before biosimilars may enter that market without risk of being sued for patent infringement. In addition, an application for a biosimilar product cannot be approved by the FDA until 12 years after the existing, branded product was approved under a Biologics License Application, or BLA. The patents for epoetin alfa, an injectable ESA, expired in 2004 in the EU, and the remaining patents expired between 2012 and 2016 in the United States. Because injectable ESAs are biologic products, the introduction of biosimilars into the injectable ESA market in the United States will constitute additional competition for vadadustat if we are able to obtain approval for and commercially launch our product. Several biosimilar versions of injectable ESAs are available for sale in the EU. In the United States, Pfizer's biosimilar version of injectable ESAs, Retacrit® (epoetin alfa-epbx), was approved by the FDA in May 2018 and launched in November 2018.

Many of our potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining marketing approvals, recruiting patients and manufacturing pharmaceutical products. Large and established companies such as Amgen and Roche, among others, compete in the market for drug products to treat kidney disease. In particular, these companies have greater experience and expertise in conducting preclinical testing and clinical trials, obtaining marketing approvals, manufacturing such products on a broad scale and marketing approved products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and have collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we are developing obsolete. Smaller and other early stage companies may also prove to be significant competitors. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or marketing approval, or discovering, developing and commercializing competitive products, before, or more effectively than, we do. If we are not able to compete effectively against potential competitors, our business will not grow and our financial condition and operations will suffer.

The commercialization of Riona in Japan, our efforts with respect to the potential commercialization of Fexeric in the EU and our current and future efforts with respect to the development and commercialization of our products and product candidates outside of the United States subject us to a variety of risks associated with international operations, which could materially adversely affect our business.

Our Japanese sublicensee, JT, and its subsidiary, Torii, commercialize Riona as an oral treatment for the improvement of hyperphosphatemia in patients with DD-CKD and NDD-CKD in Japan. While Fexeric is not currently marked in the EU, Fexeric has received conditional marketing approval in the EU as an oral treatment for the control of hyperphosphatemia in adult patients with DD-CKD and NDD-CKD, and we are continuing efforts to find a suitable commercialization partner for Fexeric in the EU. We also granted Otsuka Pharmaceutical Co. Ltd., or Otsuka, exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. In Japan and certain other countries in Asia, we granted Mitsubishi Tanabe Pharma Corporation, or MTPC, exclusive rights to commercialize vadadustat, subject to marketing approvals. We are also conducting our global Phase 3 development with respect to vadadustat for the treatment of anemia due to CKD, and MTPC is carrying out development efforts for vadadustat in Japan. As a result of these and other activities, we are or may become subject to additional risks in developing and commercializing our product and product candidates outside the United States, including:

- political, regulatory, compliance and economic developments that could restrict our ability to manufacture, market and sell our products;
- changes in international medical reimbursement policies and programs;
- changes in health care policies of foreign jurisdictions;
- trade protection measures, including import or export licensing requirements and tariffs;
- our ability to develop relationships with qualified local distributors and trading companies;
- political and economic instability in particular foreign economies and markets;
- diminished protection of intellectual property in some countries outside of the United States;
- differing labor regulations and business practices;
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and distributors' and service providers' activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, or FCPA, the UK Bribery Act or similar local regulation;
- compliance with the EU General Data Protection Regulation, or GDPR;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;

- potentially negative consequences from changes in or interpretations of tax laws;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;

- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods and fires.

Any of these factors may, individually or as a group, have a material adverse effect on our business and results of operations. As and if we continue to expand our commercialization efforts, we may encounter new risks.

Risks Related to the Clinical Development of Vadadustat and our Other Product Candidates

In addition to Auryxia, we will continue to depend heavily on the success of our product candidate, vadadustat, which is currently in Phase 3 development. Clinical drug development involves a lengthy and expensive process with an uncertain outcome. We will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and commercialization of vadadustat and any other product candidates.

The risk of failure in drug development is high. We currently have only one commercial product, Auryxia, and one product candidate, vadadustat, in clinical development, and we depend heavily on the successful commercialization of Auryxia and the successful clinical development, marketing approval and commercialization of vadadustat, which may never occur. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical trials are expensive, difficult to design and implement, can take several years to complete, and their outcomes are inherently uncertain. Failure can occur at any time during the clinical trial process. Further, the results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive or maintain marketing approval or commercialize our product candidates. Our clinical trials may take longer to complete than currently anticipated, or may be delayed, suspended, required to be repeated, prematurely terminated or may not successfully demonstrate safety and/or efficacy for a variety of other reasons, such as:

- the costs are greater than we anticipate;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate;
- enrollment in our clinical trials and accrual of MACE events may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors, such as our CRO's, may fail to comply with regulatory requirements, perform effectively, or meet their contractual obligations to us in a timely manner, or at all, or we may fail to communicate effectively or provide the appropriate level of oversight of such third-party contractors;
- the supply or quality of our starting materials, drug substance and drug product necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators, international data monitoring committees, or IDMCs, institutional review boards, or IRBs, safety committees, or ethics committees, may require that we suspend or terminate our clinical trials for various reasons, including noncompliance with regulatory requirements, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using our product candidate, or a finding that the participants are being exposed to

unacceptable health risks;

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials, repeat a clinical trial or abandon product development programs;
- lack of adequate funding to continue a clinical trial, including unforeseen costs due to enrollment delays, requirements to conduct additional clinical trials or repeat a clinical trial and increased expenses associated with the services of our CROs and other third parties;

- failure to initiate, delay of or failure to complete a clinical trial as a result of an Investigational New Drug application, or IND, being placed on clinical hold by the FDA, the EMA, the Japanese Pharmaceuticals and Medical Devices Agency, or PMDA, or other regulatory authorities, or for other reasons;
- we may determine to change or expand a clinical trial, including after it has begun;
- clinical trial sites and investigators deviating from the clinical protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial, or failure by us or our CROs to communicate effectively or provide the appropriate level of oversight of such clinical sites and investigators;
- delay or failure in having subjects complete a clinical trial or return for post-treatment follow-up;
- delay or failure in recruiting and enrolling suitable subjects to participate in a clinical trial;
- inability, delay, or failure in identifying and maintaining a sufficient number of clinical trial sites, many of which may already be engaged in other clinical programs;
- delay or failure in reaching agreement with the FDA, the EMA, PMDA or other regulatory authorities on a clinical trial design upon which we are able to execute;
- delay or failure in obtaining authorization to commence a clinical trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- delays in reaching, or failure to reach, agreement on acceptable terms with prospective clinical trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- the FDA, the EMA, PMDA or other regulatory authorities may require us to submit additional data or impose further requirements before permitting us to initiate a clinical trial or during an ongoing clinical trial;
- the FDA, the EMA, PMDA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- the design of our clinical trials;
- failure to comply with good practice quality guidelines and regulations, or GXP, including good laboratory practice, or GLP, good clinical practice, or GCP, and current good manufacturing practice, or cGMP; or
- changes in governmental regulations or administrative actions.

If we are unable to successfully complete clinical trials of our product candidates or other studies, if the results of those trials and studies are not positive or are only modestly positive, or if there are concerns with the profile due to efficacy or safety, or if any of the factors listed above occur, the following may occur:

- regulators may require that we conduct additional clinical trials, repeat clinical trials or conduct other studies of our product candidates beyond those that we currently contemplate;
- we may be delayed in obtaining marketing approval for our product candidates;
- we may not obtain marketing approval for our product candidates at all;
- we may obtain approval for indications or patient populations that are not as broad as intended or desired;
- we may obtain approval with labeling that includes significant use or distribution restrictions or safety warnings that would reduce the potential market for our products or inhibit our ability to successfully commercialize our products;
- we may be subject to additional post-marketing restrictions and/or requirements; or
- the product may be removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in preclinical and clinical development or receiving the requisite marketing approvals. Our preclinical studies or clinical trials may need to be restructured or may not be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do. This could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Even if we obtain favorable clinical results in our Phase 3 studies, we may not be able to obtain marketing approval for, or successfully commercialize, vadadustat, or we may experience significant delays in doing so, any of which would materially harm our business.

The clinical trials of our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous governmental authorities in the United States, and in other countries where we and our collaborators intend to test and, if approved, market any product candidates. Before obtaining marketing approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years and marketing approval may never be achieved. Of the large number of drugs in development in the United States and in other jurisdictions, only a small percentage successfully complete the FDA's and other jurisdictions' marketing approval processes and are commercialized. Accordingly, even if we are able to obtain the requisite capital to continue to fund our development programs, we may be unable to successfully develop or commercialize vadadustat or any other product candidates.

We and Otsuka, our collaboration partner, are not permitted to market vadadustat in the United States until we receive approval from the FDA, in the EU until we receive approval from the EMA, or in any other jurisdiction until the requisite approval from regulatory authorities in such jurisdiction is received. MTPC, our collaboration partner in Asia, will not be permitted to market vadadustat in Japan without approval from the PMDA or in any other jurisdiction until the requisite approval from regulatory authorities in such jurisdiction is received. As a condition to receiving marketing approval for vadadustat, we must complete Phase 3 studies and any additional preclinical or clinical studies required by the FDA, the EMA, PMDA or other regulatory authorities. Vadadustat may not be successful in clinical trials or receive marketing approval. Further, vadadustat may not receive marketing approval even if it is successful in clinical trials.

Obtaining marketing approval in the United States and other jurisdictions is a complex, lengthy, expensive and uncertain process that typically takes many years and depends upon numerous factors, including the substantial discretion of the regulatory authorities. Even if our product candidates demonstrate safety and efficacy in clinical studies, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain marketing approval. In addition, the safety concerns associated with injectable ESAs may affect the FDA's, EMA's, PMDA's or other regulatory authorities' review of the safety results of compounds in development for treatment of the same indications as injectable ESAs, including vadadustat. Further, the policies or regulations, or the type and amount of clinical data necessary to gain approval, may change during the course of a product candidate's clinical development and may vary among jurisdictions. It is possible that vadadustat and any other product candidates will never obtain marketing approval. The FDA may delay, limit or deny approval of vadadustat or any other product candidates for many reasons including, among others:

- we may not be able to demonstrate that vadadustat is safe and effective in treating anemia due to CKD or that any other product candidate is safe and effective for its proposed indication(s) to the satisfaction of the FDA;
- the results of our clinical trials may only be modestly positive, or there may be concerns with the profile due to efficacy or safety;
- the FDA may require us to complete both the $INNO_2VATE$ clinical program and the $PRO_2TECT$ clinical program for vadadustat prior to filing our NDA even if one of these programs finishes in advance of the other;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA for marketing approval;
- the FDA may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA may not approve the formulation, labeling or specifications we request for vadadustat or any other product candidate;
-

the FDA may approve vadadustat or any other product candidate for use only in a small patient population or for fewer or more limited indications than we request;

- the FDA may require that we conduct additional clinical trials or repeat one or more clinical trials;
- the FDA may grant approval contingent on the performance of costly post-marketing clinical trials;
- we, or our CROs or vendors, may fail to comply with GXP;
- the CROs that we retain to conduct our clinical trials may not perform effectively or take actions that adversely impact our clinical trials, or we may fail to communicate effectively or provide the appropriate level of oversight of our CROs;
- we or our third party manufacturers may fail to perform in accordance with the FDA's cGMP requirements;

- the FDA may disagree with inclusion of data obtained from certain regions outside the United States to support the NDA for potential reasons such as differences in clinical practice from United States standards;
- the FDA may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the FDA could deem that our financial relationships with certain principal investigators constitute a conflict of interest, such that the data from those principal investigators may not be used to support our applications;
- an FDA Advisory Committee or other regulatory advisory group or authority could recommend non-approval or restrictions on approval;
- the FDA's decision-making regarding vadadustat and any other product candidates may be impacted by the results of competitors' clinical trials and safety concerns of marketed products used to treat the same indications as the indications for which vadadustat and any other product candidates are being developed;
- the FDA may not approve the manufacturing processes or facilities of third party manufacturers with whom we contract; or
- the policies or regulations of the FDA may significantly change in a manner that renders our clinical data insufficient for approval, or requires us to amend or submit new clinical protocols.

In addition, similar reasons may cause the EMA or PMDA or other regulatory authorities to delay, limit or deny approval of vadadustat or any other product candidate outside the United States.

If we experience delays in obtaining approval, or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired, which could have a material adverse effect on our business.

We may find it difficult to enroll patients in our clinical studies, which could delay or prevent clinical studies of our product candidates.

Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends, in part, on the speed at which we can recruit patients to participate in testing our product candidates. Patients may be unwilling to participate in our clinical studies of vadadustat or other product candidates because of concerns about adverse events observed with injectable ESAs, other investigational agents and commercial products in CKD or for other reasons, including competitive clinical studies for similar patient populations. In addition, patients currently receiving treatment with injectable ESAs may be reluctant to participate in a clinical trial with an investigational drug. Finally, competition for clinical trial sites may limit our access to subjects appropriate for studies of vadadustat and any other product candidates. As a result, the timeline for recruiting patients, conducting studies and obtaining marketing approval of vadadustat and any other product candidates may be delayed. These delays could result in increased costs, delays in advancing our development of vadadustat and any other product candidates, or termination of the clinical studies altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical studies in a timely manner. Patient enrollment is affected by many factors, including:

- severity of the disease under investigation;
- design of the study protocol;
- size and nature of the patient population;
- eligibility criteria for, and design of, the study in question;
- perceived risks and benefits of the product candidate under study, including as a result of adverse effects observed in similar or competing therapies;
- proximity and availability of clinical study sites for prospective patients;
- availability of competing therapies and clinical studies and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to available therapies or other product candidates in

development;

57

- efforts to facilitate timely enrollment in clinical studies;
- clinical trial sites and investigators failing to perform effectively;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

We may not be able to initiate or continue clinical studies if we cannot enroll a sufficient number of eligible patients to participate in the clinical studies required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical studies as planned, we may need to delay, limit or terminate ongoing or planned clinical studies, any of which could have a material adverse effect on our business.

We may not be able to conduct clinical trials in some jurisdictions outside of the United States.

We and our collaboration partners currently expect to seek marketing approval of vadadustat for the treatment of anemia due to CKD in markets outside the United States, including the EU and Japan. Our ability to successfully initiate, enroll and complete a clinical study in any country outside of the United States is subject to numerous additional risks unique to conducting business in jurisdictions outside the United States, including:

- difficulty in establishing or managing relationships with qualified CROs, physicians and clinical trial sites;
- different local standards for the conduct of clinical studies;
- difficulty in complying with various and complex import laws and regulations when shipping drug to certain countries; and
- the potential burden of complying with a variety of laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments.

Data obtained from studies conducted in the United States may not be accepted by the EMA, PMDA and other regulatory authorities outside of the United States. Also, certain jurisdictions require data from studies conducted in their country in order to obtain approval in that country. For example, in Japan, MTPC is conducting a Phase 3 program of vadadustat, which is separate from our global Phase 3 program of vadadustat.

If we or our collaboration partners have difficulty conducting our clinical studies in jurisdictions outside the United States as planned, we may need to delay, limit or terminate ongoing or planned clinical studies, any of which could have a material adverse effect on our business.

Positive results from preclinical and clinical studies are not necessarily predictive of the results of any future clinical studies.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical studies may not be predictive of similar results in humans during clinical trials, successful results from early or small clinical trials may not be replicated in later and larger clinical trials, and successful interim results from ongoing clinical studies may not be indicative of results obtained when those studies are completed. For example, our encouraging preclinical and clinical results for vadadustat thus far do not ensure that the results of any future clinical trials will demonstrate similar results. Our global Phase 3 development program for vadadustat is enrolling a larger number of subjects and will treat subjects for longer periods than our prior trials, which will result in a greater likelihood that adverse events may be observed. Due to these and other differences between our global Phase 3 development program for vadadustat and our prior trials, our positive results from preclinical and clinical studies may not be replicated in our global Phase 3 development program for vadadustat. Many companies in the biopharmaceutical industry have suffered significant setbacks in late-stage clinical trials after achieving positive results in early stage development, and we may face similar setbacks. If the results of our ongoing or future clinical trials for vadadustat or any other product candidates are inconclusive with respect to efficacy, if we do not meet our clinical endpoints with statistical significance, or if there are safety concerns or adverse events, we may be prevented from or delayed in obtaining marketing approval for vadadustat or

any other product candidates.

We may not be successful in our efforts to identify, acquire, discover, develop and commercialize additional products or product candidates, which could impair our ability to grow.

Although we continue to focus a substantial amount of our efforts on the commercialization of Auryxia and the development and potential commercialization of vadadustat, a key element of our long-term growth strategy is to acquire, develop and/or market additional products and product candidates. Research programs to identify product candidates require substantial technical, financial and human resources, regardless of whether product candidates are ultimately identified. Our research and development programs may initially show promise, yet fail to yield product candidates for clinical development or commercialization for many reasons, including the following:

- the research methodology used may not be successful in identifying potential indications and/or product candidates;
- we may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates;
- a product candidate may be shown to have harmful side effects, a lack of efficacy or otherwise does not meet applicable regulatory criteria;
- product candidates we develop may nevertheless be covered by third-party patents or other exclusive rights;
- the market for a product candidate may change during our program so that the continued development of that product candidate is no longer reasonable;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- a product candidate may not be accepted as safe and effective by patients, the medical community, or third-party payors, if applicable.

If any of these events occurs, we may be forced to abandon our development efforts for one or more of our programs, or we may not be able to identify, discover, develop or commercialize additional product candidates, which would have a material adverse effect on our business.

Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Because our internal research capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists, and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select, and acquire promising product candidates and products. The process of proposing, negotiating and implementing a license or acquisition of a product candidate or an approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of a product candidate or an approved product. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses, and technologies and integrate them into our current infrastructure.

Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts, including, for example, with respect to the Merger. Any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA, the EMA, PMDA or other regulatory authorities, or post-approval testing or other requirements if approved. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any products that we develop or approved products that we acquire will be manufactured profitably, achieve market acceptance or not require substantial post-marketing clinical trials.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our product candidates or to acquire or develop suitable potential product candidates or approved products, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential product candidates or other programs that ultimately prove to be unsuccessful.

Auryxia, vadadustat or other products and product candidates may cause undesirable side effects or have other properties that delay or limit their commercial potential, or in the case of our product candidates, prevent their marketing approval.

Undesirable side effects caused by our product or product candidates or competing products in development that utilize a common mechanism of action could cause us or regulatory authorities to interrupt, delay or halt clinical trials, could result in a more restrictive label or the delay, denial or withdrawal of marketing approval by the FDA or other regulatory authorities, and could lead to potential product liability claims. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics.

If we or others identify undesirable side effects caused by Auryxia, vadadustat, or other products or product candidates, either before or after receipt of marketing approval, a number of potentially significant negative consequences could result, including:

- our clinical trials may be put on hold;
- patient recruitment could be slowed, and enrolled patients may not want to complete the clinical trial;
- we may be unable to obtain marketing approval for our product candidates or regulatory authorities may withdraw approvals of products;
- regulatory authorities may require warnings on the label such as the warning on Auryxia's label regarding iron overload;
- Risk Evaluation and Mitigation Strategies, or REMS, or FDA-imposed risk management plans that use risk minimization strategies to ensure that the benefits of certain prescription drugs outweigh their risks, may be required;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining marketing approval and, ultimately, market acceptance of Auryxia, vadadustat or other products or product candidates, could substantially increase our costs, and could significantly impact our ability to successfully commercialize Auryxia, vadadustat, or other products and product candidates and generate revenues.

The patient populations treated with Auryxia and the subjects in our clinical studies for vadadustat, have CKD, a serious disease that increases the risk of cardiovascular disease including heart attacks and stroke and, ultimately, may cause kidney failure. Many patients with CKD are elderly with comorbidities making them susceptible to significant health risks. Therefore, the likelihood of these subjects having adverse events, including serious adverse events, while participating in our studies is high. In our Phase 1 and Phase 2 studies of vadadustat, adverse events were reported. For example, in our Phase 2b study of vadadustat in non-dialysis subjects with anemia due to CKD, one subject with multiple co-morbidities and concomitant medications, including chlorthalidone, had a serious adverse event of liver function test abnormal, considered a case of drug induced liver injury meeting the biochemical criteria of Hy's Law, which was assessed as probably related to vadadustat. Serious adverse events considered related to vadadustat and any other product candidates could have a material adverse effect on the development of such product candidates and our business as a whole. Our understanding of adverse events in prior clinical trials of our product candidates may change as we gather more information, and additional unexpected adverse events may be observed in future clinical trials.

The most commonly reported adverse reactions in the clinical trials that supported the approval of Auryxia for the Hyperphosphatemia Indication in the United States included diarrhea (21%), discolored feces (19%), nausea (11%), constipation (8%), vomiting (7%), and cough (6%). Gastrointestinal adverse reactions were the most common reason for discontinuing Auryxia (14%) in clinical trials for the Hyperphosphatemia Indication. The most commonly reported adverse reactions in the clinical trials that supported the approval of Auryxia in the United States for the IDA Indication included discolored feces (22%), diarrhea (21%), constipation (18%), nausea (10%), abdominal pain (5%) and hyperkalemia (5%). Diarrhea was the most common reason for discontinuing Auryxia (2.6%) in clinical trials for

the IDA Indication.

Furthermore, any post-marketing clinical trials conducted, if successful, may expand the patient populations treated with Auryxia. or any other products we acquire or for which we receive marketing approval, within or outside of their current indications or patient populations, which could result in the identification of previously unknown side effects, increased frequency or severity of known side effects, or detection of unexpected safety signals. In addition, as Auryxia and any other products are commercialized, they will be used in larger patient populations and in less rigorously controlled environments than in clinical studies. As a result, regulatory authorities, healthcare practitioners, third-party payors or patients may perceive or conclude that the use of Auryxia or any other products are associated with serious adverse effects, undermining our commercialization efforts.

Further, if we or others identify previously unknown side effects, if known side effects are more frequent or severe than in the past, if we or others detect unexpected safety signals for our products or product candidates, including Auryxia, vadadustat, or any product or product candidate perceived to be similar to Auryxia, vadadustat, or our other product candidates, or if any of the foregoing are perceived to have occurred, either before or after receipt of marketing approval, a number of potentially significant negative consequences could result, including:

- sales may be impaired;
- regulatory approvals may be restricted or withdrawn;
- we may decide to, or be required to, send drug warnings or safety alerts to physicians, pharmacists and hospitals (or FDA or other regulatory authority may choose to issue such alerts), or we may decide to conduct a product recall or be requested to do so by the FDA or other regulatory authority;
- reformulation of the product, additional nonclinical or clinical studies, changes in labeling or changes to or re-approvals of manufacturing facilities may be required;
- we may be precluded from pursuing additional development opportunities to enhance the clinical profile of a product within its indicated populations, or studying the product or product candidate in additional indications and populations or in new formulations; and
- government investigations or lawsuits, including class action suits, may be brought against us.

Any of the above occurrences could delay or prevent us from achieving or maintaining marketing approval, harm or prevent sales of Auryxia or, if approved, vadadustat or other product candidates, increase our expenses and impair or prevent our ability to successfully commercialize Auryxia, vadadustat or other product candidates

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

We are subject to a complex regulatory scheme that requires significant resources to ensure compliance. Failure to comply with applicable laws could subject us to government scrutiny or government enforcement, potentially resulting in costly investigations and/or fines or sanctions, or impacting our relationships with key regulatory agencies such as the FDA or the EMA.

A variety of laws apply to us or may otherwise restrict our activities, including the following:

- laws and regulations governing the conduct of preclinical and clinical studies in the United States and other countries in which we are conducting such studies;
- laws and regulations in the United States and in countries in which we are interacting with health care providers, patients, patient organizations and other constituencies that prohibit promoting a drug prior to approval and/or reimbursement;
- laws and regulations of countries outside the United States that prohibit pharmaceutical companies from promoting prescription drugs to the general public;
- laws, regulations and industry codes that vary from country to country and govern our relationships with health care providers, patients, patient organizations, and other constituencies, prohibit certain types of gifts and entertainment, establish codes of conduct and, in some instances, require disclosure to, or approval by, regulatory authorities for us to engage in arrangements with such constituencies;
- anti-corruption and anti-bribery laws, including the FCPA, the UK Bribery Act and various other anti-corruption laws in countries outside of the United States;
- data privacy laws existing in the United States, the EU and other countries in which we operate, including the U.S. Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, the GDPR, and state privacy and data protection laws, as well as state consumer protection laws;
- federal securities laws restricting the purchase or sale of any securities while in possession of material, non-public information; and

- international trade laws, which are laws that regulate the sale, purchase, import, export, re-export, transfer and shipment of goods, products, materials, services and technology.

Compliance with these and other applicable laws and regulations requires us to expend significant resources. Failure to comply with these laws and regulations may subject us to government investigations, penalties, damages, fines, the restructuring of our operations, or the imposition of a clinical hold, any of which could materially adversely affect our business and would result in increased costs and diversion of management attention and could delay or prevent the development, regulatory approval and commercialization of our product candidates, any of which could have a material adverse effect on our business.

We may be delayed in obtaining, or be unable to obtain, marketing approval or reimbursement for vadadustat or any other product candidate in certain countries outside of the United States.

Regulatory authorities outside of the United States will require compliance with numerous and varying requirements. The approval procedures vary among jurisdictions and may involve requirements for additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a drug product must be approved for reimbursement before it can be marketed or sold in that country. In some cases, the prices that we intend to charge for our products are also subject to approval. Approval by the FDA does not ensure approval by regulatory or reimbursement authorities outside the United States, and approval by one regulatory or reimbursement authority outside the United States does not ensure approval by the FDA or any other regulatory or reimbursement authorities. However, the failure to obtain approval or reimbursement in one jurisdiction may negatively impact our ability to obtain approval or reimbursement in another jurisdiction. The marketing approval process in countries outside of the United States may include all of the risks associated with obtaining FDA approval and, in some cases, additional risks. We may not obtain such regulatory or reimbursement approvals on a timely basis, if at all. We may not be able to file for marketing approvals and may not receive the necessary approvals to commercialize our product candidates in any market. Also, favorable pricing in certain countries depends on a number of factors, some of which are outside of our control.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. On March 29, 2017, the United Kingdom formally notified the EU of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the EU. If no formal withdrawal agreement is reached between the United Kingdom and the EU, then it is expected that the United Kingdom's membership of the European Union will automatically terminate two years after the submission of the notification of the United Kingdom’s intention to withdraw from the European Union. Discussions between the United Kingdom and the EU focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the EU on March 29, 2019 without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

Since a significant proportion of the regulatory framework in the United Kingdom is derived from EU directives and regulations, the withdrawal could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the EU. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occurs, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or EU for our product candidates, which could significantly and materially harm our business.

Products approved for marketing are subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them is approved.

Marketing approvals may be subject to limitations on the approved indicated uses for which the product may be marketed or other conditions of approval, or contain requirements for potentially costly post-marketing studies and surveillance to monitor the safety and efficacy of the product, including REMS, or registries or observational studies. For example, in connection with the FDA approvals of Auryxia, we initially committed to the FDA to conduct certain post-approval pediatric studies of Auryxia under the Pediatric Research Equity Act. With regard to our Hyperphosphatemia Indication, we committed to completing the post-approval pediatric study and submitting a final report to the FDA by December 31, 2019, which was recently extended to July 2022 by the FDA in response to our request. With regards to our IDA Indication, we committed to completing the post-approval pediatric study and submitting a final report to the FDA by January 2023. We cannot guarantee that we will be able to complete these studies and submit the final reports in a timely manner. If we are unable to complete these studies successfully, our marketing approval could be suspended or revoked, which would have a material adverse impact on our ability to commercialize Auryxia and our ability to generate revenues from Auryxia. In addition, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for Auryxia, and any other product for which we receive regulatory approval, will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval.

Moreover, the FDA and other regulatory authorities closely regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory authorities impose stringent restrictions on companies' communications regarding use of their products, and if we promote our products beyond their approved indications or inconsistent with the approved label, we may be subject to enforcement actions or prosecution arising from such activities. Violations of the U.S. Federal Food, Drug, and Cosmetic Act, or the FD&C Act, relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse and other laws, as well as state consumer protection laws, third-party payor actions, shareholder actions and other lawsuits.

Post-approval discovery of previously unknown problems with an approved product, including adverse events of unanticipated severity or frequency or relating to manufacturing operations or processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing, distribution, use or manufacturing of the product;
- withdrawal of the product from the market, or product recalls;
- restrictions on the labeling or marketing of a product;
- fines, restitution or disgorgement of profits or revenues;
- warning or untitled letters or clinical holds;
- refusal by the FDA or other regulatory authorities to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- REMS; and
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with FDA, EMA, PMDA and other regulatory authorities' requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties.

The FDA's policies and those of other regulatory authorities may change, and additional government regulations may be enacted. We cannot predict the likelihood, nature or extent of government regulations that may arise from future legislation or administrative action, either in the United States or in other jurisdictions. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would materially adversely affect our business.

We will incur significant liability if it is determined that we are promoting any "off-label" use of Auryxia or if it is determined that any of our activities violates the federal Anti-Kickback Statute.

Physicians are permitted to prescribe drug products for uses that differ from those approved by the FDA or other applicable regulatory agencies. Although the FDA and other regulatory agencies do not regulate a physician's choice of treatments, the FDA and other regulatory agencies do restrict manufacturer communications regarding unapproved uses of an approved drug. Companies are not permitted to promote drugs for unapproved uses or in a manner that is inconsistent with the FDA-approved labeling. There are also restrictions about making comparative or superiority claims based on safety or efficacy that are not supported by substantial evidence. Accordingly, we may not promote Auryxia in the United States for use in any indications other than the Hyperphosphatemia Indication and the IDA Indication, and all promotional claims must be consistent with the FDA-approved labeling for Auryxia. Promoting a drug off-label is a violation of the FD&C Act and can give rise to liability under the federal False Claims Act, as well as under additional federal and state laws and insurance statutes. The FDA and other regulatory and enforcement authorities enforce laws and regulations prohibiting promotion of off-label uses and the promotion of products for which marketing approval has not been obtained, as well as the false advertising or misleading promotion of drugs. In

addition, laws and regulations govern the distribution and tracing of prescription drugs and prescription drug samples, including the Prescription Drug Marketing Act of 1976 and the Drug Supply Chain Security Act, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the U.S. federal level and set minimum standards for the regulation of drug distributors by the states. A company that is found to have improperly promoted off-label uses or to have otherwise engaged in false or misleading promotion or improper distribution of drugs will be subject to significant liability, potentially including civil and administrative remedies as well as criminal sanctions.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. In addition, under some relatively recent guidances from the FDA, companies may also promote information that is consistent with the prescribing information and proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug. We intend to engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. Although we believe we have put in place a robust compliance program and processes designed to ensure that all such activities are performed in a legal and compliant manner, Auryxia is our first commercial product so our implementation of our compliance program in connection with commercialization activities is still relatively new.

In addition, if a company's activities are determined to have violated the federal Anti-Kickback Statute, this can also give rise to liability under the federal False Claims Act and such violations can result in significant fines, criminal and civil remedies, and exclusion from Medicare and Medicaid. There is increased government focus on relationships between the pharmaceutical industry and physicians, pharmacies (especially specialty pharmacies), and other sources of referrals. Common industry activities, such as speaker programs, insurance assistance and support, relationships with foundations providing copayment assistance, and relationships with patient organizations and patients are receiving increased governmental attention. If any of our relationships or activities is determined to violate applicable federal and state anti-kickback laws, false claims laws, or other laws or regulations, the company and/or company executives and other representatives could be subject to significant fines and criminal sanctions, imprisonment, and potential exclusion from Medicare and Medicaid.

Recent efforts to pursue regulatory reform may limit the FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

Recently, there have been several executive actions taken, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, an executive order, applicable to all executive agencies including the FDA, was issued that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. Interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and Budget on February 2, 2017, indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

We are conducting global clinical trials in countries where corruption is prevalent. In addition, we are subject to a variety of import and export trade laws. Violations of any of these laws by our personnel or by any of our vendors or agents, such as our CROs or CMOs, could have a material adverse impact on our clinical trials and our business and could result in criminal or civil fines and sanctions.

We are subject to complex laws that govern our international business practices. These laws include the FCPA, which prohibits U.S. companies and their intermediaries, such as CROs or CMOs, from making improper payments to

foreign government officials for the purposes of obtaining or keeping business or to obtain any kind of advantage for the company. The FCPA also requires companies to keep accurate books and records and maintain adequate accounting controls. A number of past and recent FCPA investigations by the Department of Justice and the U.S. Securities and Exchange Commission have focused on the life sciences sector.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. Some of the countries in which we are conducting clinical trials have a history of corruption, which increases our risks of FCPA violations. In addition, the FCPA presents unique challenges in the pharmaceutical industry because in many countries hospitals are operated by the government, and doctors and other hospital employees are considered foreign government officials. Certain payments made by pharmaceutical companies, or on their behalf by CROs, to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Additionally, the UK Bribery Act applies to our global activities and prohibits bribery of private individuals as well as public officials. The UK Bribery Act prohibits both the offering and accepting a bribe and imposes strict liability on companies for failing to prevent bribery, unless the company can show that it had "adequate procedures" in place to prevent bribery. There are also local anti-bribery and anti-corruption laws in countries where we are conducting clinical trials, and many of these also carry the risk of significant financial or criminal penalties.

We are also subject to trade control regulations and trade sanctions laws that restrict the movement of certain goods, currency, products, materials, services and technology to, and certain operations in, various countries or with certain persons. Our ability to transfer people and products among certain countries is subject to maintaining required licenses and complying with these laws and regulations.

The internal controls, policies and procedures, and training and compliance programs we have implemented to deter prohibited practices may not be effective in preventing our employees, contractors, consultants, agents or other representatives from violating or circumventing such internal policies or violating applicable laws and regulations. The failure to comply with laws governing international business practices may impact our clinical trials, result in substantial civil or criminal penalties for us and any such individuals, including imprisonment, suspension or debarment from government contracting, withdrawal of our products, if approved, from the market, or being delisted from The Nasdaq Global Market. In addition, we may incur significant costs in implementing sufficient systems, controls and processes to ensure compliance with the aforementioned laws.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the EU. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations. Similarly, failure to comply with federal and state laws regarding privacy and security of personal information could expose us to fines and penalties under such laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Our relationships with healthcare providers, physicians and third-party payors are subject to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of Auryxia and any other product candidates for which we obtain marketing approval. Our arrangements with healthcare providers, physicians and third-party payors expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute Auryxia and any other product candidates for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by federal and state governments and by governments in foreign jurisdictions in which we conduct our business. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the FD&C Act which among other things, strictly regulates drug product marketing and promotion and prohibits manufacturers from marketing such products for off-label use;
- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs, and laws requiring notification of price increases;
- the federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $5,500 to $11,000 per false claim;
- HIPAA imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the HITECH, and their respective implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and gift ban and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and which are not preempted by federal laws and often differ from state to state, thus complicating compliance efforts; and
- U.S. state laws restricting interactions with healthcare providers and other members of the healthcare community or requiring pharmaceutical manufacturers to implement certain compliance standards.

Because of the breadth of these U.S. laws, and their non-U.S. equivalents, and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent healthcare reforms have strengthened these laws. For example, the Health Care Reform Act, among other things, amended the intent requirement of the federal anti-kickback law. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate the law. The Health Care Reform Act also amended the False Claims Act, such that violations of the anti-kickback statute are now deemed violations of the False Claims Act.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, such as the Pharmaceutical Research and Manufacturers of America Code on Interactions with Health Care Professionals, known as the PhRMA Code. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government funded healthcare programs.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain for any products that are approved in the United States or foreign jurisdictions.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell Auryxia and any product candidates for which we obtain marketing approval. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. Current laws, 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 receive for any FDA approved product, such as Auryxia.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for Auryxia and any other approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA. Among the provisions of the ACA of potential importance to our business including, without limitation, our ability to commercialize and the prices we obtain for Auryxia and may obtain for any of our product candidates that are approved for sale, are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal anti-kickback statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% starting January 1, 2019) point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
-

new requirements to report certain financial arrangements with physicians and teaching hospitals;

- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year which will remain in effect through 2027 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for Auryxia or any product candidates for which we may obtain regulatory approval or the frequency with which Auryxia and any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

With the enactment of the Tax Cuts and Jobs Act of 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause an estimated 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, the President signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole”. Further, each chamber of the U.S. Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA.

The current administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, the President has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, the U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor

payments to third-party payors who argued that such payments were owed to them. The effects of this gap in reimbursement on third-party payors, providers, and potentially our business, are not yet known.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States, and members of U.S. Congress and the current administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Including measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Specifically, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the current administration issued a plan to lower drug prices. Under this blueprint for action, the current administration indicated that the Department of Health and Human Services, or HHS, will take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies, advance biosimilars and generics to boost price competition, evaluate the inclusion of prices in drug makers' ads to enhance price competition, speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers, avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid, work to give Medicare Part D plan sponsors more negotiation power with drug makers, examine which Medicare Part B drug prices could be negotiated by Medicare Part D plans, improve the design of the Medicare Part B Competitive Acquisition Program, update Medicare's drug-pricing dashboard to increase transparency, prohibit Medicare Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance, and require that Medicare Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. More recently, on January 31, 2019, the HHS Office of Inspector General proposed modifications to the federal anti-kickback statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products or put pressure on our product pricing.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for Auryxia and any product candidates for which we receive marketing approval or additional pricing pressures. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for Auryxia and any products candidates for which we receive marketing approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain and maintain coverage and reimbursement approval for Auryxia or any other approved product;
- our ability to generate revenues and achieve or maintain profitability; and
- the level of taxes that we are required to pay.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the use and disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from the use of hazardous materials by our employees, contractors or consultants, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to our Reliance on Third Parties

If the licensor of certain intellectual property relating to Auryxia terminates, modifies or threatens to terminate existing contracts or relationships with us, our business may be materially harmed.

We do not own the rights to our product, Auryxia. We have licensed and sublicensed the rights, patent or otherwise, to Auryxia from a third-party, Panion, who in turn licenses certain rights to Auryxia from one of the inventors of Auryxia. The license agreement with Panion requires us to meet development milestones and imposes development and commercialization due diligence requirements on us. In addition, under the license agreement, we must pay royalties based on a mid-single digit percentage of net sales of product resulting from the licensed technologies, including Auryxia and pay the patent filing, prosecution and maintenance costs related to the license. If we do not meet our obligations in a timely manner, or if we otherwise breach the terms of our license agreement, Panion could terminate the agreement, and we would lose the rights to Auryxia. For example, following announcement of the Merger, Panion notified Keryx in writing that Panion would terminate the license agreement on November 21, 2018 if Keryx did not cure the breach alleged by Panion, specifically, that Keryx failed to use commercially reasonable best efforts to commercialize Auryxia outside the United States. Keryx disagreed with Panion's claims, and the parties entered discussions to resolve this dispute. On October 24, 2018, prior to the consummation of the Merger, we, Keryx and Panion entered into a letter agreement, or the Panion Letter Agreement, pursuant to which Panion agreed to rescind any and all prior termination threats or notices relating to the license agreement and waived its rights to terminate the license agreement based on any breach by us of our obligation to use commercially reasonable efforts to commercialize Auryxia outside the United States until the parties execute an amendment to the license agreement, in accordance with the terms of the Panion Letter Agreement, following consummation of the Merger. These terms of the amendment to the license agreement include establishing a joint steering committee consisting of Panion and our representatives to oversee the development and commercialization of Fexeric in Europe and providing Panion with an exclusive license under Keryx-owned patents covering the rights to make, use, sell, offer for sale and import ferric citrate in certain countries in the Asia-Pacific region. The parties intend to work together to agree on a commercialization plan for Fexeric in Europe following execution of the amendment to the license agreement. The amendment to the license agreement is expected to include alternatives in the event a commercialization plan is not agreed upon, such as payment of an annual license maintenance fee to Panion or the return of European intellectual property rights to Panion. In addition, under the terms of the Panion Letter Agreement, Panion has agreed that we will have the right, but not the obligation, to conduct any litigation against any infringer of patent rights under the license agreement on the terms agreed upon in the Panion Letter Agreement. Keryx made a $500,000 payment to Panion in connection with the execution of the Panion Letter Agreement. Even though we entered into the Panion Letter Agreement, there are no assurances that we will successfully negotiate with Panion with respect to the regulatory and commercial plans for Fexeric in Europe, that an amendment to the license agreement will be entered into or that Panion will not allege other breaches of the license agreement or otherwise attempt to terminate the license agreement in the future.

In addition, if Panion breaches its agreement with the inventor from whom it licenses rights to Auryxia, Panion could lose its license, which could impair or delay our ability to develop and commercialize Auryxia.

From time to time, we may have disagreements with Panion, or Panion may have disagreements with the inventor from whom it licenses rights to Auryxia, regarding the terms of the agreements or ownership of proprietary rights, which could impact the commercialization of Auryxia, could require or result in litigation or arbitration, which would be time-consuming and expensive, could lead to the termination of our license agreement with Panion, or force us to negotiate a revised or new license agreement on terms less favorable than the original. In addition, in the event that the owners and/or licensors of the rights we license were to enter into bankruptcy or similar proceedings, we could potentially lose our rights to Auryxia or our rights could otherwise be adversely affected, which could prevent us from continuing to commercialize Auryxia.

We rely on third parties to conduct preclinical and clinical studies for our product candidates. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to commercialize Auryxia or obtain marketing approval for or commercialize vadadustat or any other product candidates, and our business could be substantially harmed.

We do not have the ability to independently conduct preclinical and clinical trials. We are currently relying, and expect to continue to rely, on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our current and future preclinical studies and our clinical trials, including our global Phase 3 development program for vadadustat. The third parties on whom we rely may fail to perform effectively, or terminate their engagement with us, for a number of reasons, including the following:

- if the quantity or accuracy of the data obtained by the third parties is compromised due to their failure to adhere to clinical trial protocols or to regulatory requirements, or if the third parties otherwise fail to comply with clinical trial protocols, perform effectively or meet expected deadlines;
- if third parties experience staffing difficulties;
- if we fail to communicate effectively or provide the appropriate level of oversight;
- if third parties undergo changes in priorities or corporate structure or become financially distressed; or
- if they form relationships with other entities, some of which may be our competitors.

Any of these events could cause our preclinical and clinical trials, including post-approval clinical trials, to be extended, delayed, suspended, required to be repeated or terminated, or we may receive untitled warning letters or be the subject of an enforcement action which could result in our failing to obtain marketing approval of vadadustat or any other product candidates on a timely basis, or at all, or fail to maintain marketing approval of Auryxia or any other approved products, any of which would adversely affect our business operations. In addition, if the third parties on whom we rely fail to perform effectively or terminate their engagement with us, we may need to enter into alternative arrangements, which could delay, perhaps significantly, the continued commercialization of Auryxia and the development and commercialization of vadadustat and any other product candidates.

Even though we do not directly control the third parties on whom we rely to conduct our preclinical and clinical trials and therefore cannot guarantee the satisfactory and timely performance of their obligations to us, we are nevertheless responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements, including GXP requirements, and scientific standards, and our reliance on these third parties, including CROs, will not relieve us of our regulatory responsibilities. If we or any of our CROs, their subcontractors, or clinical trial sites fail to comply with applicable GXP requirements, the clinical data generated in our clinical trials may be deemed unreliable or insufficient, our clinical trials could be put on hold, and/or the FDA, the EMA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with drug product that meets certain specifications and is manufactured under applicable cGMP regulations. These requirements include, among other things, quality control, quality assurance, and the satisfactory maintenance of records and documentation.

We also rely on third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, resulting in additional costs and depriving us of potential product revenue. In addition, we are using an active comparator in our $PRO_2TECT$ and $INNO_2VATE$ clinical programs for vadadustat. If our distributors are unable to obtain sufficient supply of the active comparator for any reason, or supply active comparator to clinical trial sites in a timely manner, our clinical trials may be extended, delayed, suspended or terminated.

We rely on third parties to conduct all aspects of our product manufacturing. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to continue commercializing Auryxia or obtain marketing approval for or commercialize vadadustat or any other product candidates, and our business could be substantially harmed.

We do not have any manufacturing facilities and do not expect to independently manufacture any product or product candidates. We currently rely on third party manufacturers to produce all of our commercial, preclinical and clinical material supply. We expect to continue to rely on existing or alternative third party manufacturers to supply our ongoing and planned preclinical and clinical trials and for commercial production. We currently have multiple suppliers of Auryxia's drug substance and one supplier with three approved sites for the supply of Auryxia drug product. If any of our suppliers were to limit or terminate production, or otherwise fail to meet the quality or delivery requirements needed to supply Auryxia at adequate levels, we could experience losses of revenue which could materially and adversely impact our results of operations. We plan to enter into agreements with third party manufacturers to manufacture commercial quantities of drug substance and drug product for vadadustat; however, we may not be able to negotiate these agreements at commercially reasonable terms. For example, a contract manufacturer may require a substantial financial commitment, including but not limited to a commitment to fund the purchase of a new facility or equipment. Our reliance on third party manufacturers increases the risk that we will not have sufficient quantities of our product candidates or the ability to obtain such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

As a result of the large quantity of materials required for Auryxia production and the large quantities of Auryxia tablets that are required for our commercial success, the commercial viability of Auryxia will also depend on adequate supply of starting materials that meet quality, quantity and cost standards and the ability of our contract manufacturers to continually produce drug substance and finished drug product on a commercial scale. Failure to achieve and maintain these levels of supply can jeopardize and prevent the successful commercialization of Auryxia. Moreover, issues that may arise in our scale-up and technology transfer of Auryxia and continued commercial scale manufacture of Auryxia may lead to significant delays in our development and commercial timelines and negatively impact our financial performance. For example, a production-related issue resulted in an interruption in the supply of Auryxia in the third and fourth quarters of 2016. This supply interruption negatively impacted Keryx's revenues in 2016. Although this supply interruption was resolved and actions designed to prevent future interruptions in the supply of Auryxia have been taken, any future supply interruptions for Auryxia or any of our product candidates for which we receive marketing approval would negatively and materially impact our reputation and financial condition.

If any of our third-party manufacturers cannot perform as agreed, including a misappropriation of our proprietary information, or if they terminate their engagements with us, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into agreements with other third party manufacturers, which we may not be able to do on favorable or reasonable terms, if at all. In some cases, there may be a limited number of qualified replacement manufacturers, or the technical skills, or equipment required to manufacture a product or product candidate may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party or a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture Auryxia or our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to continue to commercialize or satisfy patient demand for Auryxia or any other product candidate for which we receive marketing approval, or develop and receive marketing approval for our product candidates in a timely manner or within budget.

The facilities and processes used by our third party manufacturers to manufacture Auryxia may be inspected by the FDA and other regulatory authorities at any time, and the facilities and processes used by our third party manufacturers to manufacture our product candidates will be inspected by the FDA, the EMA and other regulatory authorities prior to or after we submit our marketing application. We do not control the manufacturing processes of, and are completely dependent on, our third party manufacturers for compliance with cGMP requirements for manufacture of certain starting materials, drug substance and finished drug product. If our third party manufacturers cannot successfully manufacture material that conforms to our specifications and regulatory requirements, we will not be able to maintain marketing approval for Auryxia or secure and/or maintain marketing approval for our product candidates. In addition, we have no control over the ability of our third party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, the EMA or other regulatory authorities do not approve the facilities being used to manufacture f our product candidates, or if they withdraw any approval of the facilities being used to manufacture Auryxia or any other product candidates for which we receive marketing approval, we may need to find alternative manufacturing facilities, which would significantly impact our ability to continue commercializing Auryxia or develop, obtain marketing approval for or market our product candidates, if approved. Moreover, the failure of our third party manufacturers to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of Auryxia or our product candidates operating restrictions or criminal prosecutions, any of which could significantly and adversely affect the supply of Auryxia or our product candidates. Also, if our starting materials,

drug substance or drug product are damaged or lost while in our third party manufacturers' control, it may impact our ability to supply our products or product candidates and we may incur significant financial harm. In addition, Auryxia and our product candidates may compete with other products and product candidates and products for access to third party manufacturing facilities. A third party manufacturer may also encounter delays brought on by sudden internal resource constraints, labor disputes, or shifting regulatory protocols. Certain of these third party manufacturing facilities may be contractually prohibited from manufacturing our product candidates or products, due to exclusivity provisions in agreements with our competitors. There are a limited number of manufacturers that operate under cGMP regulations and are capable of manufacturing Auryxia and our product candidates for us.

Our current and anticipated future dependence on third parties for the manufacture of Auryxia and our product candidates may adversely affect our ability to continue to commercialize Auryxia or any product candidates that receive marketing approval on a timely and competitive basis and any future profit margins.

Third party manufacturers may be unable to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products.

In order to complete our development of and commercialize, if approved, vadadustat and any other product candidates, we will need to work with third party manufacturers to manufacture them in large quantities. Our current and future third party manufacturers may be unable to successfully achieve commercial scale production of vadadustat or increase the manufacturing capacity of any other product candidates for the conduct of clinical trials and commercialization in a timely or cost-effective manner, if at all. In addition, quality issues may arise during scale-up activities. Any changes in our manufacturing processes as a result of scaling up may result in the need to obtain additional marketing approvals. If our third party manufacturers are unable to achieve commercial scale production or there is a need for additional marketing approvals of vadadustat or any other product candidates, or if there are difficulties in increasing the manufacturing capacity for any other product candidates, the development, marketing approval and commercialization of that product candidate may be delayed or infeasible, or ongoing commercialization may be unsuccessful, any of which could significantly harm our business.

The loss of any of our manufacturers could materially harm our business.

We currently have redundant supply arrangements in place for the commercial supply of Auryxia and the preclinical and clinical supply of vadadustat. While we intend to put redundant supply arrangements in place for commercial manufacturing of vadadustat, we may be unsuccessful in doing so due to a number of factors, including that we may not be able to negotiate binding agreements at commercially reasonable terms. Even if we are ultimately successful in entering into redundant supply arrangements for commercial manufacturing of vadadustat, the timing of such arrangements is uncertain.

We do not know whether our third party manufacturers will be able to meet our demand, either because of the nature of our agreements with those third party manufacturers, or, in some cases, our limited experience with those third party manufacturers or our relative importance as a customer to those third party manufacturers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our current third party manufacturers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers.

If we are unsuccessful in implementing redundant supply arrangements for commercial quantities of vadadustat or if our commercial supply arrangements for Auryxia are terminated, or if any of our third party manufacturers is unable to fulfill the terms of their agreements with us, are subject to regulatory review, or cease their operations for any reason, it could result in delays to our marketing approval and risk that we would not have sufficient quantities of our

product candidates and products for clinical trials and commercialization.

We depend on collaborations with third parties for the development and commercialization of vadadustat and Auryxia. If our collaborations are not successful or if our collaborators terminate their agreements with us, we may not be able to capitalize on the market potential of Auryxia and vadadustat, and our business could be materially harmed.

We sublicensed the rights to commercialize Riona, the trade name for ferric citrate in Japan, to Japan Tobacco, Inc., or JT, and its subsidiary Torii Pharmaceutical Co., Ltd., or Torii, in Japan. We entered into collaboration agreements with Otsuka to develop and commercialize vadadustat in the United States, Europe, China and certain other territories. We also entered into a collaboration agreement with MTPC to develop and commercialize vadadustat in Japan and certain other Asian countries. We may form or seek other strategic alliances, joint ventures, or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our commercialization efforts with respect to Auryxia and our development and commercialization efforts with respect to vadadustat and any other product candidates. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

We may not be able to maintain our collaborations and our collaborations may not be successful due to a number of important factors, including the following:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborations may be terminated in accordance with the terms of the collaborations and, if terminated, may make it difficult for us to attract new collaborators or adversely affect how we are perceived in scientific and financial communities, and may result in a need for additional capital and expansion of our internal capabilities to pursue further development or commercialization of the applicable products and product candidates;
- if permitted by the terms of the collaborations, collaborators may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus, availability of funding or other external factors such as a business combination that diverts resources or creates competing priorities;
- if permitted by the terms of the collaborations, collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- a collaborator with marketing and distribution rights our products may not commit sufficient resources to their marketing and distribution;
- if permitted by the terms of the collaboration, we and our collaborator may have a difference of opinion regarding the development or commercialization strategy for a particular product, and our collaborator may have ultimate decision making authority;
- disputes may arise between a collaborator and us that cause the delay or termination of activities related to research, development or commercialization of Auryxia, vadadustat and any other product candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may not lead to development or commercialization of products and product candidates in the most efficient manner or at all;
- a significant change in the senior management team, a change in the financial condition or a change in the business operations, including a change in control or internal corporate restructuring, of any of our collaborators, could result in delayed timelines, re-prioritization of our programs, decreasing resources or funding allocated to support our programs, or termination of the collaborations; and
- collaborators may not comply with all applicable regulatory requirements.

If any of these events occurs, the market potential of our products and product candidates could be reduced, and our business could be materially harmed. We also cannot be certain that, following a collaboration, the benefits of the collaboration will outweigh the potential risks.

We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

We will require substantial additional cash to fund the continued commercialization of Auryxia and the development and potential commercialization of vadadustat and any other product candidates. We may decide to enter into additional collaborations for the development and commercialization of vadadustat or Auryxia. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business.

We may not be successful in entering into additional collaborations as a result of many factors including the following:

- competition in seeking appropriate collaborators;
- a reduced number of potential collaborators due to recent business combinations in the pharmaceutical industry;
- inability to negotiate collaborations on acceptable terms;

- inability to negotiate collaborations on a timely basis;
- a potential collaborator's evaluation of our product or product candidates;
- a potential collaborator's resources and expertise; and
- restrictions due to an existing collaboration agreement.

If we are unable to enter into additional collaborations, we may have to curtail the commercialization of the product or the development of the product candidate on which we are seeking to collaborate, reduce or delay its development program or other of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further commercialize Auryxia or develop or commercialize our product candidates.

Even if we enter into additional collaboration agreements and strategic partnerships or license our intellectual property, we may not be able to maintain them or they may be unsuccessful, which could delay our timelines or otherwise adversely affect our business.

Risks Related to our Intellectual Property

If we are unable to adequately protect our intellectual property, third parties may be able to use our intellectual property, which could adversely affect our ability to compete in the market.

Our commercial success will depend in part on our ability, and the ability of our licensors, to obtain and maintain patent protection on our drug product and technologies, and to successfully defend these patents against third-party challenges. We seek to protect our proprietary products and technology by filing patent applications in the United States and certain foreign jurisdictions. The process for obtaining patent protection is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications in a cost effective or timely manner. In addition, we may fail to identify patentable subject matter early enough to obtain patent protection. Further, license agreements with third parties may not allow us to control the preparation, filing and prosecution of patent applications, or the maintenance or enforcement of patents. Such third parties may decide not to enforce such patents or enforce such patents without our involvement. Thus, these patent applications and patents may not under these circumstances, be prosecuted or enforced in a manner consistent with the best interests of the company.

Our pending patent applications may not issue as patents and may not issue in all countries in which we develop, manufacture or potentially sell our product(s) or in countries where others develop, manufacture and potentially sell products using our technologies. Moreover, our pending patent applications, if issued as patents, may not provide additional protection for our product.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in pharmaceutical and biotechnology patents has emerged to date. Changes in the patent laws or the interpretation of the patent laws in the United States and other jurisdictions may diminish the value of our patents or narrow the scope of our patent protection. Accordingly, the patents we own or license may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative drug products or technologies or design around our patented drug product and technologies which may have an adverse effect on our business. If our competitors prepare and file patent applications in the United States that claim technology also claimed by us, we may have to participate in interference or derivation proceedings in front of the U.S. Patent and Trademark Office, or USPTO, to determine priority of invention, which could result in substantial cost, even if the eventual outcome is favorable to us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that any related patent may expire prior to, or remain in existence for only a short period following, commercialization, thus reducing any advantage of the patent. The patents we own or license may be challenged or invalidated or may fail to provide us with any competitive advantage. Since we have licensed or sublicensed many patents from third parties, we may not be able to enforce such licensed patents

against third-party infringers without the cooperation of the patent owner and the licensor, which may not be forthcoming. In addition, we may not be successful or timely in obtaining any patents for which we submit applications.

Additionally, the laws of foreign countries may not protect our intellectual property rights to the same extent as do the laws of the United States. For example, claims in a patent application directed to methods of treatment of the human body are not patentable or are restricted in many non-U.S. countries. Further, we may not pursue or obtain patent protection in all major markets. In addition, in jurisdictions outside the United States where we own or license patent rights, we may be unable to prevent unlicensed parties from selling or importing products or technologies derived elsewhere using our proprietary technology.

Generally, the first to file a patent application is entitled to the patent if all other requirements of patentability are met. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Since publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Moreover, the laws enacted by the Leahy-Smith America Invents Act of 2011, or the Act, which reformed certain patent laws in the United States, introduce procedures that permit competitors to challenge our patents in the USPTO after grant, including inter partes review and post grant review. Similar laws exist outside of the United States. The laws of the European Patent Convention, for example, provide for post-grant opposition procedures that permit competitors to challenge, or oppose, our European patents administratively at the European Patent Office.

On November 25, 2015, a third party filed an opposition to our issued European Patent No. 1 931 689, or the ‘689 EP Patent, which covers Fexeric. During the oral proceedings, which took place on June 27, 2017, the Opposition Division of the European Patent Office, or EPO, revoked the ‘689 EP Patent. On December 6, 2017, we filed an appeal of the decision of the Opposition Division, which is presently pending. According to European practice, the revocation of the patent is stayed until an appeal is finally resolved. We anticipate the appeal will take a few years to resolve, during which time the patent will remain in force.

On December 23, 2016, a third party filed an opposition to our issued European Patent No. 1 978 807, or the ’807 EP Patent, which covers Fexeric. During the oral proceedings, which took place on June 8, 2018, the Opposition Division of the EPO maintained the ’807 EP Patent as granted. This decision resulted in the maintenance of all of the claims of the patent, including claims directed to the use of ferric citrate for preventing, reversing, maintaining or delaying progression of chronic kidney disease. On November 16, 2018, the third party filed an appeal of the decision of the Opposition Division, which is presently pending. We anticipate the appeal will take a few years to resolve.

In July 2011, a third party filed an opposition to our issued European patents, European Patent No. 2044005, or the ’005 EP Patent, which covers vadadustat. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office decided to maintain certain claims of the patent directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases including, but not limited to, anemia. Both parties appealed the decision of the Opposition Division. On February 27, 2018, we withdrew the ’005 EP Patent from appeal and filed a divisional patent application to pursue a focused claim set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia. We cannot be assured that such claims in the divisional application will be granted by the European Patent Office. If such claims are not granted, or the scope of the claims is significantly narrowed, we may not be able to adequately protect our rights, provide sufficient exclusivity, or preserve our competitive advantage.

We may become involved in addressing patentability objections based on third-party submission of references, or we may become involved in defending our patent rights in oppositions, derivation proceedings, reexamination, inter partes review, post grant review, interference proceedings or other patent office proceedings or litigation, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse result in any such proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged on such a basis in the courts or patent offices in the United States and abroad. As a result of such challenges, we may lose exclusivity or freedom-to-operate or patent claims may be narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to prevent third parties from using or commercializing similar or identical products, or limit the duration of the patent protection for our products.

In addition, patents protecting our product candidate might expire before or shortly after such candidate is commercialized. Thus, our patent portfolio may not provide sufficient rights to exclude others from commercializing products similar or identical to ours.

We also rely on trade secrets and know-how to protect our intellectual property where we believe patent protection is not appropriate or obtainable. Trade secrets are difficult to protect. While we require our employees, licensees, collaborators and consultants to enter into confidentiality agreements, this may not be sufficient to adequately protect our trade secrets or other proprietary information. In addition, we share ownership and publication rights to data relating to our drug product and technologies with our research collaborators and scientific advisors. If we cannot maintain the confidentiality of this information, our ability to receive patent protection or protect our trade secrets or other proprietary information will be at risk.

The intellectual property that we own or have licensed relating to our product, Auryxia, is limited, which could adversely affect our ability to compete in the market and adversely affect the value of Auryxia.

The patent rights that we own or have licensed relating to Auryxia are limited in ways that may affect our ability to exclude third parties from competing against us. For example, a third-party may design around our owned or licensed composition of matter patent claims or not market a product for methods of use covered by our owned or licensed patents.

Obtaining proof of direct infringement by a competitor for a method of use patent requires us to demonstrate that the competitors make and market a product for the patented use(s). Alternatively, we can prove that our competitors induce or contribute to others in engaging in direct infringement. Proving that a competitor contributes to, or induces, infringement of a patented method by another has additional proof requirements. For example, proving inducement of infringement requires proof of intent by the competitor. If we are required to defend ourselves against claims or to protect our own proprietary rights against others, it could result in substantial costs to us and the distraction of our management. An adverse ruling in any litigation or administrative proceeding could prevent us from marketing and selling Auryxia, increase the risk that a generic or other similar version of Auryxia could enter the market to compete with Auryxia, limit our development and commercialization of Auryxia, or otherwise harm our competitive position and result in additional significant costs. In addition, any successful claim of infringement asserted against us could subject us to monetary damages or injunction, which could prevent us from making or selling Auryxia. We also may be required to obtain licenses to use the relevant technology. Such licenses may not be available on commercially reasonable terms, if at all.

Moreover, physicians may prescribe a competitive identical product for indications other than the one for which the product has been approved, or “off-label” indications, that are covered by the applicable patents. Although such off-label prescriptions may directly infringe or contribute to or induce infringement of method of use patents, such infringement is difficult to prevent.

In addition, any limitations of our patent protection described above may adversely affect the value of our drug product and may inhibit our ability to obtain a collaboration partner at terms acceptable to us, if at all.

In the United States, the FDA has the authority to grant additional regulatory exclusivity protection for approved drugs where the sponsor conducts specified testing in pediatric or adolescent populations. If granted, this pediatric exclusivity may provide an additional six months which are added to the term of any non-patent exclusivity that has been awarded as well as to the regulatory protection related to the term of a relevant patent, to the extent these protections have not already expired.

In addition to patent protection, we may utilize, if granted by the FDA, pediatric exclusivity or other provisions of the FDCA such as new chemical entity, or NCE, exclusivity, or exclusivity for a new use or new formulation, to provide non-patent market exclusivity for a drug product. The FDCA provides a five-year period of non-patent exclusivity within the United States to the first applicant to gain approval of a new drug application, or NDA, for an NCE. A drug is an NCE if the FDA has not previously approved any other new drug containing the same active moiety, which consists of the molecule(s) or ion(s) responsible for the action of the drug substance (but not including those portions of the molecule that cause it to be a salt or ester or which are not bound to the molecule by covalent or similar bonds). During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an ANDA or 505(b)(2) NDA that references an NDA product with NCE exclusivity may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application (for example, for new indications, dosages, or strengths of an existing drug). This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. The three-year exclusivity period, unlike five-year exclusivity, does not prevent the submission of a competing ANDA or 505(b)(2) NDA. Instead, it only prevents the FDA from granting final approval to such a product until expiration of the exclusivity period. Five-year and three-year exclusivity will not delay the submission (in the case of five-year exclusivity) or the approval (in the case of three-year exclusivity) of a full NDA submitted under section 505(b)(1) of the FDCA; however, an applicant submitting a full NDA would be

required to conduct all of its own studies needed to independently support a finding of safety and effectiveness for the proposed product, or have a full right of reference to all studies not conducted by the applicant.

On August 23, 2018, Keryx submitted a Citizen Petition requesting, inter alia, that FDA recognize that Auryxia is eligible for five years of new chemical entity, or NCE, exclusivity based on its novel active ingredient and for three years exclusivity for the IDA Indication. On January 19, 2019, FDA responded that Auryxia is eligible for a three-year exclusivity period for the IDA Indication, which expires on November 6, 2020. FDA, however, denied the NCE exclusivity based on its determination that Auryxia contains a previously-approved active moiety (ferric cation). FDA's decision on the Citizen Petition is subject to further review both within FDA and in the courts. On February 21, 2019, we filed a Petition for Reconsideration of FDA's decision on the NCE determination for Auryxia.

We cannot assure that Auryxia or any drug candidates we may acquire or in-license will obtain such pediatric exclusivity, NCE exclusivity or any other market exclusivity in the United States, EU or any other territory, or that we will be the first to receive the respective regulatory approval for such drugs so as to be eligible for any market exclusivity protection. We also cannot assure that Auryxia or any drug candidates we may acquire or in-license will obtain patent term extension.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to assist with research, development and manufacture of our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, services agreements, material transfer agreements, consulting agreements, research agreements or other similar agreements with our advisors, employees, third-party contractors, collaborators and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such information becomes known by our competitors, is inadvertently incorporated into the technology of others, or is disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors, and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution with which we may collaborate will usually expect to be granted rights to publish data arising out of such collaboration. We often grant such rights, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration and remove confidential or trade secret information from any such publication. In the future, we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties or independent development or disclosure or publication of information by any of our employees, advisors, consultants, third-party contractors or collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Litigation or third-party claims of intellectual property infringement may be costly and time consuming and may delay or harm our drug discovery, development and commercialization efforts.

We may be forced to initiate litigation to enforce our contractual and intellectual property rights, or we may be sued by third parties asserting claims based on contract, tort or intellectual property infringement. In addition, third parties may have or may obtain patents in the future and claim that our product or any other technologies infringe their patents. If we are required to defend against suits brought by third parties, or if we sue third parties to protect our rights, we may be required to pay substantial litigation costs, and our management's attention may be diverted from operating our business. In addition, any legal action against our licensor or us that seeks damages or an injunction of our commercial activities relating to our product or other technologies could subject us to monetary liability, a temporary or permanent injunction preventing the development, marketing and sale of our product or such technologies, and/or require our licensor or us to obtain a license to continue to use our product or other technologies. We cannot predict whether our licensor or we would prevail in any of these types of actions or that any required license would be made available on commercially acceptable terms, if at all.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. The pharmaceutical and biotechnology industries are characterized by extensive litigation over patent and other intellectual property rights. We have in the past and may in the future become a party to, or be threatened with, future adversarial litigation or other proceedings regarding intellectual property rights with respect to our drug candidates. As the pharmaceutical and biotechnology industries expand and more patents are issued, the risk increases

that our drug candidates may give rise to claims of infringement of the patent rights of others.

While our product candidates are in preclinical studies and clinical trials, we believe that the use of our product candidates in these preclinical studies and clinical trials in the United States falls within the scope of the exemptions provided by 35 U.S.C. Section 271(e), which provides that it shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention solely for uses reasonably related to the development and submission of information to the FDA. As a result of the Merger, our portfolio now includes a commercial product, Auryxia. Consequently, there is an increased possibility of a patent infringement claim against us. We attempt to ensure that our product candidates and the methods we employ to manufacture them, as well as the methods for their use which we intend to promote, do not infringe other parties' patents and other proprietary rights. There can be no assurance they do not, however, and competitors or other parties may assert that we infringe their proprietary rights in any event.

Third parties may hold or obtain patents or other intellectual property rights and allege in the future that the use of our products or product candidates infringes these patents or intellectual property rights, or that we are employing their proprietary technology without authorization. We do not believe that there are any currently issued U.S. patents that will prevent us from commercializing Auryxia or vadadustat; nor do we make any admission that any of such patents are valid, enforceable or infringed. Under U.S. law, a party may be able to patent a discovery of a new way to use a previously known compound, even if such compound itself is patented, provided the newly discovered use is novel and nonobvious. Such a method-of-use patent, however, if valid, only protects the use of a claimed

compound for the specified methods claimed in the patent. This type of patent does not prevent persons from using the compound for any previously known use of the compound. Further, this type of patent does not prevent persons from making and marketing the compound for an indication that is outside the scope of the patented method. We are not aware of any valid U.S. patents issued to FibroGen, or any other person, that claim methods of using any of our product candidates for purposes of inhibiting hypoxia-inducible factor prolyl hydroxylases, or HIF-PHs, for the treatment of anemia due to CKD. For example, we are aware of certain patents that have been acquired by FibroGen directed to certain heterocyclic carboxamide compounds that are described as inhibitors of prolyl-4-hydroxylase. Those patents, however, are believed to have expired as of December 2014.

FibroGen has also filed other patent applications in the U.S. and other countries directed to purportedly new methods of using such previously known heterocyclic carboxamide compounds for purposes of treating or affecting specified conditions, and some of these applications have since issued as patents. To the extent any such patents issue or have been issued, we may initiate opposition or other legal proceedings with respect to such patents. We discuss the status of the opposition and/or invalidation proceedings against certain FibroGen patents in Part I, Item 3. Legal Proceedings of this Annual Report on Form 10-K.

There may be other patents of FibroGen or patents of other third parties of which we are currently unaware with claims to compounds, materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our drug candidates. Also, because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe.

Third parties, including FibroGen, may in the future claim that our product candidates and other technologies infringe upon their patents and may challenge our ability to commercialize vadadustat. Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to continue to commercialize Auryxia or further develop and commercialize vadadustat or any other product candidates. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our products or product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product or product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or our intended methods of use, including patient selection methods, the holders of any such patent may be able to block or impair our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. We may also elect to enter into a license in order to settle litigation or in order to resolve disputes prior to litigation. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our products or product candidates. Should a license to a third-party patent become necessary, we cannot predict whether we would be able to obtain a license or, if a license were available, whether it would be available on commercially reasonable terms. If such a license is necessary and a license under the applicable patent is unavailable on commercially reasonable terms, or at all, our ability to commercialize our products or product candidates may be impaired or delayed, which could in turn significantly harm our business.

Further, defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties or redesign our products, which may be impossible or require substantial time and monetary expenditure.

We are currently involved in patent infringement lawsuits and opposition and invalidity proceedings and may in the future be involved in additional lawsuits or administrative proceedings to challenge the patents of our competitors or to protect or enforce our patents, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or misappropriate our trade secrets or confidential information. To counter infringement or unauthorized use, we may be required to file infringement or misappropriation claims, which can be expensive and time-consuming. We may not be able to prevent infringement of our patents or misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and held not infringed and could put our patent applications at risk of not issuing.

In addition, there may be a challenge or dispute regarding inventorship or ownership of patents or applications currently identified as being owned by or licensed to us. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. Interference proceedings provoked by third parties or brought by the US PTO may be necessary to determine the priority of inventions with respect to our patents or patent applications.

Various administrative proceedings are also available for challenging patents, including interference, reexamination, inter partes review, and post-grant review proceedings before the US PTO or oppositions and other comparable proceedings in foreign jurisdictions. An unfavorable outcome in any current or future proceeding in which we are challenging third-party patents could require us to cease using the patented technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all. Even if we are successful, participation in interference or other administrative proceedings before the US PTO or a foreign patent office may result in substantial costs and distract our management and other employees.

For example, we are currently involved in patent infringement lawsuits against several generic companies in the District Courts of Delaware and West Virginia. In addition, we are currently involved in opposition or invalidation proceedings in the European Patent Office, the Japan Patent Office, the Canadian Federal Court and the United Kingdom Patents Court. These proceedings may be ongoing for a number of years and may involve substantial expense and diversion of employee resources from our business. In addition, we may become involved in additional opposition proceedings or other legal or administrative proceedings in the future. For more information, see the other risk factors under “Risks Related to our Intellectual Property” and Part I, Item 3. Legal Proceedings of this Annual Report on Form 10-K.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation and some administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure during discovery. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the US PTO and foreign patent agencies in several stages over the lifetime of the patent. The US PTO and governmental patent agencies in other jurisdictions also require compliance with a number of procedural, documentary, fee payment (such as annuities) and other similar provisions during the patent application process. While an inadvertent lapse in many cases can be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from potential collaborators, prospective licensees and other third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees’ former employers. We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in

developing our product candidates. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. Consequently, the breadth of our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the United States. As a result, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other countries. Competitors may use our technologies in countries where we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories where we have patent protection, but enforcement is not as strong as in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to pharmaceutical and biotechnology products, 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 countries outside of the United States could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks Related to our Business and Industry

If we fail to attract, keep and motivate senior management and key personnel, we may be unable to successfully develop vadadustat and commercialize Auryxia.

Recruiting and retaining qualified scientific, clinical, medical, manufacturing and sales and marketing personnel is critical to our success. We are also highly dependent on our executives, certain members of our senior management and certain members of our commercial organization. The loss of the services of our executives, senior managers or other key employees, including employees in our commercial organization, could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executives, senior managers and other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain marketing approval of and commercialize products. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel, particularly in our geographic region.

We also experience competition for the hiring of personnel from universities and research institutions. In addition, we rely on contractors, consultants and advisors, including scientific and clinical advisors, to assist us in formulating and executing our research and development and commercialization strategy. Our contractors, consultants and advisors may become employed by companies other than ours and may have commitments with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to grow and pursue our business strategy will be limited.

We may expend our limited resources to pursue a particular product, product candidate or indication and fail to capitalize on products, product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on products, research programs and product candidates for specific indications. As a result, we may forgo or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Security breaches and unauthorized use of our IT systems and information, or the IT systems or information in the possession of our collaborators and other third-parties, could damage the integrity of our clinical studies, impact our regulatory filings, compromise our ability to protect our intellectual property, and subject us to regulatory actions that could result in significant fines or other penalties.

We, our collaborators, contractors and other third-parties rely significantly upon information technology, and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business effectively. In addition, we, and our collaborators, contractors and other third parties rely on information technology networks and systems, including the Internet, to process, transmit and store clinical trial data, patient information, and other electronic information, and manage or support a variety of business processes, including operational and financial transactions and records, personal identifying information, payroll data and workforce scheduling information. We purchase some of our information technology from vendors, on whom our systems depend. We rely on commercially available systems, software, tools and monitoring to provide security for the processing, transmission and storage of company and customer information.

In the ordinary course of our business, we and our third-party contractors maintain personal and other sensitive data on our and their respective networks, including our intellectual property and proprietary or confidential business information relating to our business and that of our clinical trial subjects and business partners. In particular, we rely on CROs and other third parties to store and manage information from our clinical trials. We also rely on third parties to manage patient information for Auryxia. The secure maintenance of this sensitive information is critical to our business and reputation.

Companies and other entities and individuals have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access to systems and information. These threats can come from a variety of sources, ranging in sophistication from individual hackers to state-sponsored attacks. Cyber threats may be broadly targeted, or they may be custom-crafted against our information systems or those of our vendors or third-party service providers. A security breach, cyber-attack or unauthorized access of our clinical data or other data could damage the integrity of our clinical trials, impact our regulatory filings, cause significant risk to our business, compromise our ability to protect our intellectual property, and subject us to regulatory actions, including under the GDPR discussed elsewhere in these risk factors and the privacy or security rules under federal, state, or other international laws protecting confidential information, that could be expensive to defend and could result in significant fines or other penalties. Cyber-attacks can include malware, computer viruses, hacking or other unauthorized access or other significant compromise of our computer, communications and related systems. Although we take steps to manage and avoid these risks and to be prepared to respond to attacks, our preventive and any remedial actions may not be successful and no such measures can eliminate the possibility of the systems improper functioning or the improper access or disclosure of confidential or personally identifiable information such as in the event of cyber-attacks. Security breaches, whether through physical or electronic break-ins, computer viruses, ransomware, impersonation of authorized users, attacks by hackers or other means, can create system disruptions or shutdowns or the unauthorized disclosure of confidential information.

Likewise, although we believe our collaborators, vendors and service providers, such as our CROs, take steps to manage and avoid information security risks and respond to attacks, we may be vulnerable to attacks against our collaborators, vendors or service providers, and we may not have adequate contractual remedies against such collaborators, vendors and service providers in such event. Additionally, outside parties may attempt to fraudulently induce employees, collaborators, or other contractors to disclose sensitive information or take other actions, including making fraudulent payments or downloading malware, by using “spoofing” and “phishing” emails or other types of attacks. Our employees may be targeted by such fraudulent activities. Outside parties may also subject us to distributed denial of services attacks or introduce viruses or other malware through “trojan horse” programs to our users’ computers in order to gain access to our systems and the data stored therein. In the recent past, cyber-attacks have become more prevalent and much harder to detect and defend against and, because the techniques used to obtain unauthorized access, disable or degrade service, or sabotage systems change frequently and continuously become more sophisticated, often are not recognized until launched against a target and may be difficult to detect for a long time, we may be unable to anticipate these techniques or to implement adequate preventive or detective measures, and we might not immediately detect such incidents and the damage caused by such incidents.

Such attacks, whether successful or unsuccessful, or other compromises with respect to our information security and the measures we implement to prevent, detect and respond to them, could result in our incurring significant costs related to, for example, rebuilding internal systems, defending against litigation, responding to regulatory inquiries or actions, paying damages or fines, or taking other remedial steps with respect to third parties, divert the attention of our management and key information technology resources, disrupt key business operations, harm our reputation and deter business partners from working with us. A compromise with respect to our information security could lead to public exposure of personal information of our clinical trial subjects, Auryxia patients and others, and publicity about information security. Publicity about vulnerabilities and attempted or successful incursions could damage the integrity of our studies or delay their completion. If a compromise to our information security were to occur and cause

interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, any loss of clinical trial data could result in delays in our regulatory approval efforts for our product candidates and significantly increase our costs to recover or reproduce the data. In addition, such attacks could compromise our ability to protect our trade secrets and proprietary information from unauthorized access or misappropriation and a loss of, or damage to, our data or marketing applications. Inappropriate public disclosure of confidential or proprietary information could subject us to liability and cause delays in our product research, development and commercialization efforts. We currently do not maintain cybersecurity insurance to protect against losses due to security breaches.

Any failure to maintain proper functionality and security of our internal computer and information systems could result in a loss of, or damage to, our data or marketing applications or inappropriate disclosure of confidential or proprietary information, interrupt our operations, damage our reputation, subject us to liability claims or regulatory penalties, under a variety of federal, state or other applicable privacy laws, such as HIPAA, the GDPR, or state data protection laws, harm our competitive position and delay the further development and commercialization of our products and product candidates, or impact our relationships with Auryxia patients.

Our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate applicable laws, including the following:

- the FDA and other healthcare authorities' regulations, including those laws that require the reporting of true, complete and accurate information to regulatory authorities, and those prohibiting the promotion of unapproved drugs or approved drugs for an unapproved use;
- quality standards, including GXP;
- federal and state healthcare fraud and abuse laws and regulations and their non-U.S. equivalents;
- anti-bribery and anti-corruption laws, such as the FCPA and the UK Bribery Act or country-specific anti-bribery or anti-corruption laws, as well as various import and export laws and regulations;
- laws that require the reporting of true and accurate financial information and data; and
- U.S. securities laws and regulations and their non-U.S. equivalents.

These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. It is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity 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, or if any such action is instituted against our employees, consultants, vendors or principal investigators, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, curtailment of our operations, disclosure of our confidential information and imprisonment, any of which could adversely affect our ability to operate our business and our results of operations.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we commercialize Auryxia and advance our product candidates through clinical trials and commercialization, we have expanded and may need to further expand our clinical, medical, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. In addition, we may encounter difficulties in managing the expanded operations of a larger and more complex company following the Merger as well as challenges associated with managing an increasingly diversified business.

We have strategic collaborations for the commercialization of Riona and the development and commercialization of vadadustat. As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, consultants, vendors, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management.

In addition, in connection with the Merger, we have experienced and may to continue to experience significant growth in our employee base for sales, marketing, operational, managerial, financial, human resources, compliance, drug development, quality, regulatory and medical affairs and other areas. This growth has imposed and will continue to impose significant added responsibilities on members of management, including the need to recruit, hire, retain,

motivate and integrate additional employees, including employees who joined us in connection with the Merger. Also, our management may have to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities, including the integration of Keryx's business with our business.

Our future financial performance and our ability to commercialize Auryxia and vadadustat or any other product candidate, if approved, and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To manage our recent and anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. In addition, we may need to adjust the size of our workforce as a result of changes to our expectations for our business, which can result in diversion of management attention, disruptions to our business, and related expenses. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company or realizing the anticipated benefits of the Merger.

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

We face an inherent risk of product liability as a result of the use of our products commercially, and clinical testing of our product candidates, and we will face an even greater risk if we commercialize any additional products in the future. For example, we may be sued if any of our products or product candidates allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product or product candidate, negligence, strict liability and breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products and product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, product liability claims may result in:

- decreased demand for any product or product candidates;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- delay or termination of clinical trials;
- our inability to continue to develop a product candidate;
- significant costs to defend the related litigation;
- a diversion of management’s time and our resources;
- substantial monetary awards to study subjects or patients;
- product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- decreased demand for a product or product candidate;
- loss of revenue;
- the inability to commercialize any product or product candidates; and
- a decline in our stock price.

Failure to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance that we believe is appropriate for our company. Although we maintain product liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have insufficient or no coverage. If we have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, we may not have, or be able to obtain,

sufficient capital to pay such amounts. In addition, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost. We also may not be able to obtain additional insurance coverage that will be adequate to cover product liability risks that may arise. Consequently, a product liability claim may result in losses that could be material to our business.

Risks Related to our Common Stock

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012. As a result, take advantage of certain reduced disclosure requirements.

We are an “emerging growth company”, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and will remain an emerging growth company until December 31, 2019. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and obtaining shareholder approval of any golden parachute payments not previously approved.

Investors may find our common stock less attractive if we continue to rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

If, we are unable to satisfy the requirements of Section 404 of the Sarbanes-Oxley Act or our internal control over financial reporting is not effective, the reliability of our financial statements may be questioned and our stock price may suffer.

Section 404 of the Sarbanes-Oxley Act requires any company subject to the reporting requirements of the U.S. securities laws to do a comprehensive evaluation of its and its consolidated subsidiaries’ internal controls over financial reporting. Additionally, Section 404(b), which is applicable as of 12/31/2019, requires our independent auditors to opine on the design and operating effectiveness of our internal controls over financial reporting. The rules governing the standards that must be met for management to assess our internal controls over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act. If our management cannot favorably assess the effectiveness of our internal controls over financial reporting or our auditors identify material weaknesses in our internal controls, investor confidence in our financial results may weaken and our stock price may suffer.

Our stock price has been and may continue to be volatile, which could result in substantial losses for purchasers of our common stock and lawsuits against us and our officers and directors.

Our stock price has been and will likely continue to be volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. Since our initial public offering in March 2014, the price of our common stock as reported on The Nasdaq Global Market has ranged from a low of $5.20 on December 24, 2018 to a high of $31.00 on June 20, 2014. The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, developments related to and results of our clinical studies, developments related to our regulatory submissions, developments related to our ability to

commercialize Auryxia and any other approved product candidates, announcements by us or our competitors of significant mergers, acquisitions, licenses, strategic collaborations, joint ventures, collaborations or capital commitments, negative publicity around Auryxia, vadadustat or any other product or product candidate, the results of competitive clinical trials, products or technologies, regulatory or legal developments in the United States and other countries, developments or disputes concerning patent applications, issued patents or other proprietary rights, the recruitment or departure of key personnel, the level of expenses related to Auryxia, vadadustat or any other product or product candidate or clinical development programs, actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts, variations in our financial results or those of companies that are perceived to be similar to us, changes in the structure of healthcare payment systems, market conditions in the pharmaceutical and biotechnology sectors, general economic, industry and market conditions and others beyond our control. As a result of this volatility, our shareholders may not be able to sell their common stock at or above the price at which they purchased it.

In addition, companies that have experienced volatility in the market price of their stock have frequently been the subject of securities class action and shareholder derivative litigation. See Part I, Item 3. Legal Proceedings for information concerning securities class action and shareholder derivative lawsuits initiated against us, Keryx and certain current and former directors and officers of ours and Keryx's. In addition, we could be the target of other such litigation in the future. Class action and shareholder derivative lawsuits, whether successful or not, could result in substantial costs, damage or settlement awards and a diversion of our management's resources and attention from running our business, which could materially harm our reputation, financial condition and results of operations.

The issuance of additional shares of our common stock or the sale of shares of our common stock by any of our directors, officers or significant shareholders will dilute our shareholders' ownership interest in Akebia and may cause the market price of our common stock to decline.

Most of our outstanding common stock can be traded without restriction at any time. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell such shares, could reduce the market price of our common stock.

Baupost Group Securities, L.L.C., or Baupost, beneficially owns approximately 21% of our outstanding common stock, and our former director Muneer Satter owns approximately 3% of our outstanding common stock. Subject to certain restrictions, Baupost and Mr. Satter are able to sell their shares of common stock in the public market from time to time without registering them, subject to certain limitations on the timing, amount and method of those sales imposed by Rule 144 under the Securities Act of 1933, as amended. In addition, pursuant to our registration rights agreement with Baupost and our Fourth Amended and Restated Investor Rights Agreement, as amended, with Mr. Satter, Baupost and Mr. Satter have the right, subject to certain conditions and with certain exceptions, to require us to file registration statements covering the shares common stock they own or to include their shares in registration statements that we may file or in public offerings of our shares of common stock. Following their registration and sale under the applicable registration statement, those shares would become freely tradable. By exercising their registration rights and selling a large number of shares of common stock, Baupost and Mr. Satter could cause the price of our common stock to decline.

We have a significant number of shares that are subject to outstanding options, restricted stock units and warrants, and in the future we may issue additional options, restricted stock units, warrants or other derivative securities convertible into our common stock. The exercise or vesting of any such options, restricted stock units, warrants or other derivative securities, and the subsequent sale of the underlying common stock, could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. Also, the Merger was financed by the issuance of shares of our common stock to shareholders of Keryx, comprising approximately 50.6% of our issued and outstanding shares of common stock, calculated based on our fully diluted market capitalization as of the date of signing the Agreement and Plan of Merger relating to the Merger. Keryx shareholders may decide not to hold the shares of our common stock they received in the Merger. Other Keryx shareholders, such as funds with limitations on the amount of stock they are permitted to hold in individual issuers, may be required to sell the shares of our common stock they received in the Merger. Such sales of our common stock could result in higher than average trading volume and may cause the market price for our common stock to decline.

In addition, we currently have on file with the SEC universal shelf registration statements, which allow us to offer and sell certain registered securities, such as common stock, preferred stock, warrants and units, from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. Also, on May 23, 2016, we entered into a sales agreement with Cantor Fitzgerald, pursuant to which, from time to time, we may offer and sell through Cantor Fitzgerald up to an aggregate of $75.0 million of the common stock pursuant to one or more "at the

market," or ATM, offerings. In addition, with our prior written approval, Cantor Fitzgerald may sell these shares of common stock by any other method permitted by law, including in privately negotiated transactions. As of December 31, 2018, we have sold $41.0 million of our common stock pursuant to two ATM facilities.

Sales of substantial amounts of shares of our common stock or other securities by our employees or our other shareholders or by us pursuant to the ATM, under our universal shelf registration statements or otherwise could dilute our stockholders, lower the market price of our common stock and impair our ability to raise capital through the sale of equity securities.

Insiders and significant stockholders could cause us to take actions that may not be, or refrain from taking actions that may be, in our best interest or in the best interest of all of our stockholders.

As of February 28, 2019, we believe that our directors and executive officers, together with their affiliates, beneficially owned, in the aggregate, approximately 3% of our outstanding common stock, In addition, we have certain significant stockholders, including Baupost, which owns approximately 21% of our outstanding common stock. As a result, if certain significant stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs, such as:

- the composition of our Board of Directors;
- the adoption of amendments to our Ninth Amended and Restated Certificate of Incorporation and Amended and Restated By-Laws;
- the approval of mergers or sales of substantially all of our assets;
- our capital structure and financing; and
- the approval of contracts between us and these shareholders or their affiliates, which could involve conflicts of interest.

This concentration of ownership could harm the market price of our common stock by:

- delaying, deferring or preventing a change in control of our company and making some transactions more difficult or impossible without the support of these stockholders, even if such transactions are beneficial to other stockholders;
- impeding a merger, consolidation, takeover or other business combination involving our company; or
- entrenching our management or our Board of Directors.

Moreover, the interests of these stockholders may conflict with the interests of other stockholders, and we may be required to engage in transactions that may not be agreeable to or in the best interest of us or other stockholders.

We will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, and particularly following December 31, 2019 when we will no longer be an “emerging growth company”, we will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, or the SOX Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and make some activities more time-consuming and costly, especially since we will no longer be an “emerging growth company” after December 31, 2019 and we will therefore no longer be able to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are “emerging growth companies”.

We cannot predict or estimate the amount of additional costs we may incur to continue to operate as a public company, nor can we predict the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies, which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other

public reporting which would harm our business and the trading price of our common stock.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us, as and when required, conducted in connection with Section 404 of the SOX, or Section 404, or any subsequent testing by our independent registered public accounting firm, as and when required, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. As a larger company following the Merger, implementing and maintaining effective controls may require more resources, and we may encounter internal control integration difficulties. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

Pursuant to Section 404, are required to furnish a report by our management on our internal control over financial reporting. However, as an "emerging growth company", we have not been required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm until we are no longer an emerging growth company as of January 1, 2020. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Provisions in our organizational documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our Ninth Amended and Restated Certificate of Incorporation, Amended and Restated By-Laws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our Board of Directors is responsible for appointing certain members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our Board of Directors. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by our Board of Directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified Board of Directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our Board of Directors pursuant to a resolution adopted by a majority of the total number of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our Board of Directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our Board of Directors may be filled only by a majority of directors then in office, even though less than a quorum;
- require a supermajority vote of 75% of the holders of our capital stock entitled to vote or the majority vote of our Board of Directors to amend our Amended and Restated By-Laws; and
- require a supermajority vote of 85% of the holders of our capital stock entitled to vote to amend the classification of our Board of Directors and to amend certain other provisions of our Ninth Amended and Restated Certificate of Incorporation.

These provisions, alone or together, could delay or prevent hostile takeovers, changes in control or changes in our management.

In addition, Section 203 of the Delaware General Corporation Law prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is

approved in a prescribed manner.

Any provision of our Ninth Amended and Restated Certificate of Incorporation, our Amended and Restated By-Laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our ability to use net operating losses to offset future taxable income may be subject to certain limitations.

Under Section 382 of the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, to offset future taxable income. On December 12, 2018, we completed the Merger, which we believe has resulted in a change in control under Section 382 of the Code, or Section 382. Future changes in our stock ownership, many of which are outside of our control, could result in an additional ownership change under Section 382. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Furthermore, our ability to utilize our NOLs is conditioned upon our attaining profitability and generating U.S. taxable income. As described above under "—Risks Related to our Financial Position and Need for Additional Capital," we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the U.S. income necessary to utilize our NOLs. A valuation allowance has been provided for the entire amount of our NOLs.

Our Ninth Amended and Restated Certificate of Incorporation designates the state or federal courts located in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our Ninth Amended and Restated Certificate of Incorporation provides that, subject to limited exceptions, the state and federal courts located in the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our Ninth Amended and Restated Certificate of Incorporation or our Amended and Restated By-Laws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. Under our Ninth Amended and Restated Certificate of Incorporation, this exclusive forum provision will not apply to claims that are vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery of the State of Delaware, or for which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. For instance, the provision would not apply to actions arising under federal securities laws, including suits brought to enforce any liability or duty created by the Exchange Act or the rules and regulations thereunder. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our Ninth Amended and Restated Certificate of Incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our Ninth Amended and Restated Certificate of Incorporation inapplicable to, or unenforceable with respect to, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

We are currently subject to securities class action litigation and other legal proceedings, which could result in substantial costs and divert management's attention, and we could be subject to additional securities class actions, shareholder derivative lawsuits and other legal proceedings.

We are currently subject to securities class action litigation and other legal proceedings as described in Part I, Item 3. Legal Proceedings. In addition, securities class action and derivative lawsuits and other legal proceedings are often brought against companies for any of the risks described in this Annual Report on Form 10-K following a decline in the market price of their securities. In connection with any litigation or other legal proceedings, we could incur substantial costs, and such costs and any related settlements or judgments may not be covered by insurance. We could also suffer an adverse impact on our reputation and a diversion of management's attention and resources, which could have a material adverse effect on our business.

Because we do not anticipate paying any cash dividends on our capital in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. In addition, the terms of our current or future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

Item 1B. Unresolved Staff Comments
None

Item 2. Properties
Our corporate headquarters are located in Cambridge, Massachusetts. We currently lease approximately 65,167 square feet of office and lab space in Cambridge, Massachusetts, and 27,300 square feet of office space in Boston, Massachusetts. Excluding renewal options, the lease for the Cambridge, Massachusetts office space expires on September 11, 2026, the lease for the Cambridge, Massachusetts lab space expires on November 30, 2021, and the lease for the Boston, Massachusetts office space expires on February 28, 2023. By the end of 2019, we plan to move employees based in our Boston office to our Cambridge office and sublet our Boston office. We believe that our existing facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms for our future growth.

Item 3. Legal Proceedings
Shareholder Litigation

Shareholder Litigation Relating to our Merger with Keryx

On June 28, 2018, we entered into an Agreement and Plan of Merger with Keryx Biopharmaceuticals, Inc., or Keryx, and Alpha Therapeutics Merger Sub, Inc., or the Merger Sub, pursuant to which the Merger Sub would merge with and into Keryx, with Keryx becoming a wholly owned subsidiary of ours, or the Merger. On December 12, 2018, we completed the Merger. In October and November 2018, four purported shareholders of Keryx filed four separate putative class actions, or the Merger Securities Actions, against Keryx, a former officer and director of Keryx (Jodie P. Morrison, who is now a director of ours), former directors of Keryx (Kevin J. Cameron, Mark J. Enyedy, Steven C. Gilman, Michael T. Heffernan, Daniel P. Regan and Michael Rogers, some of whom are current members of our Board of Directors), and, with respect to one action, the Merger Sub and Akebia, challenging the disclosures made in connection with the Merger. The complaints in the Merger Securities Actions generally allege that the registration statement filed in connection with the Merger failed to disclose certain allegedly material information in violation of Section 14(a) and 20(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and Rule 14a-9 promulgated thereunder. The alleged omissions relate to (i) certain financial projections for Keryx and Akebia and certain financial analyses performed by our advisors; (ii) certain terms relating to the engagement of one of Keryx's advisors; and (iii) any alleged negotiations that may have taken place regarding which individuals would serve on our Board of Directors after consummation of the Merger as well as future employment of officers. Each of the complaints seeks to enjoin the defendants from proceeding with the Merger; however, none of the plaintiffs filed a motion seeking such relief before the Merger was consummated. The complaints also seek rescission of the Merger or rescissory damages, a declaration that that the defendants violated Sections 14(a) and 20(a) of the Exchange Act and Rule 14a-9 thereunder, and an award of plaintiffs' costs, including reasonable allowance for attorneys' fees and experts' fees.

Three of the Merger Securities Actions are pending in the United States District Court for the District of Delaware, or the Delaware District Court: Corwin v. Keryx Biopharmaceuticals, Inc., et al. (filed October 16, 2018); Van Hulst v.

Keryx Biopharmaceuticals, Inc., et al. (filed October 24, 2018); and Andreula v. Keryx Biopharmaceuticals, Inc., et al. (filed November 1, 2018). On January 4, 2019, plaintiff John Andreula filed a motion to consolidate the three actions pending in the Delaware District Court and appoint himself as lead plaintiff. The Delaware District Court has yet to rule on that motion. The fourth Merger Securities Action was filed in the United States District Court for the District of Massachusetts, or the Massachusetts District Court: Rosenblatt v. Keryx Biopharmaceuticals, Inc., et al. (filed October 23, 2018). The plaintiff in the Rosenblatt action filed a notice of voluntary dismissal of the action without prejudice, on February 19, 2019.

On December 10, 2018, a purported stockholder of Keryx, Michael J. Donnelly, filed a complaint against Keryx pursuant to Section 220 of the Delaware General Corporation Law in the Delaware Court of Chancery, captioned Donnelly v. Keryx Biopharmaceuticals, Inc., or the Donnelly Action. The Donnelly Action seeks inspection of various Keryx books and records, purportedly to investigate "possible wrongdoing," in connection with Keryx's negotiation and approval of the Merger, as well as the independence of former members of Keryx's Board of Directors, some of whom are current members of our Board of Directors. In addition to the production of books and records, the Donnelly Action seeks costs and expenses incurred in the action, including reasonable attorneys' fees. On January 31, 2019, Keryx answered the complaint in the Donnelly Action. To date, no schedule has been ordered in the Donnelly Action.

Shareholder Litigation Relating to Auryxia Supply

Four putative class action lawsuits have been filed against Keryx and certain of its former officers (Gregory P. Madison, Scott A. Holmes, Ron Bentsur, and James Oliviero) and consolidated in the Massachusetts District Court, captioned Karth v. Keryx Biopharmaceuticals, Inc., et al. (filed October 26, 2016, with an amended complaint filed on February 27, 2017). Plaintiffs seek to represent all stockholders who purchased shares of Keryx common stock between May 8, 2013 and August 1, 2016. The complaint alleges that Keryx and the named individual defendants violated Sections 10(b) and/or 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning Keryx, its supplier relationships, and future prospects, and that the allegedly misleading statements were not made known to the market until Keryx's August 1, 2016 announcement of an interruption in its supply of Auryxia. By order dated July 19, 2018, the Massachusetts District Court granted in part and denied in part the defendants' motion to dismiss the complaint. The parties are presently engaged in discovery. No trial date has been set.

Two stockholder derivative complaints also were filed on December 16, 2016 against Keryx and certain of its former officers (Gregory P. Madison, Scott A. Holmes, Ron Bentsur and James Oliviero) certain of its former directors (Kevin J. Cameron, Daniel P. Regan, Steven C. Gilman, Michael Rogers Michael P. Tarnok, Joseph Feczko, Jack Kaye Wyche Fowler, Jr. and John P. Butler), some of whom are current directors and officers of ours, in the Superior Court of Massachusetts, one captioned Venkat Vara Prasad Malledi v. Keryx Biopharmaceuticals, Inc., et al., and one captioned James Anderson v. Keryx Biopharmaceuticals, Inc., et al.. Each of these two complaints generally alleges breach of fiduciary duty, unjust enrichment, abuse of control, mismanagement and corporate waste. On June 27, 2017, the Superior Court of Massachusetts granted the parties' motion to consolidate and stay the derivative litigations. All of the complaints seek unspecified damages, interest, attorneys' fees, and other costs.

We deny any allegations of wrongdoing and intend to vigorously defend against the shareholder lawsuits described in this section. There is no assurance, however, that we will be successful in the defense of these lawsuits or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of these actions. Moreover, we are unable to predict the outcome or reasonably estimate a range of possible losses at this time. A resolution of these lawsuits in a manner adverse to us, however, could have a material effect on our financial position and results of operations in the period in which a particular lawsuit is resolved.

Legal Proceedings Relating to Auryxia

ANDA Litigation

On October 31, 2018, November 6, 2018, December 24, 2018 and February 4, 2019, Keryx received Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the U.S. Food and Drug Administration, or FDA, by Lupin Atlantis Holdings SA, or Lupin, Teva Pharmaceuticals USA, Inc., or Teva, Chemo Research S.L., or Chemo, and Mylan Pharmaceuticals Inc., or Mylan, respectively, requesting approval for generic versions of Auryxia tablets (210 mg iron per tablet). On December 13, 2018, Keryx and its licensors, Panion & BF Biotech, Inc., or Panion, and Chen Hsing Hsu, M.D., filed a complaint for patent infringement against Lupin and Lupin Ltd., or the Lupin Defendants, in the Delaware District Court, arising from Lupin's ANDA filing with the FDA. On December 19, 2018, Keryx and Panion filed a complaint for patent infringement against Teva and Teva Pharmaceutical Industries Limited, or the Teva Defendants, in the Delaware District Court arising from Teva's ANDA filing with the FDA. On February 1, 2019, Keryx, Panion and Dr. Hsu filed a complaint for patent infringement against Chemo and Insud Pharma S.A., or the Chemo Defendants, in the Delaware District Court arising from Chemo's ANDA filing with the FDA. On March 15, 2019, Keryx, Panion and Dr. Hsu filed a complaint for patent infringement against Mylan in the United States District Court for the Northern District of West Virginia of arising from Mylan's ANDA filing with the FDA.

As a result of the timely filing of these lawsuits in accordance with the relevant statute, a 30-month stay of approval will be imposed by the FDA on Lupin's, Teva's, Chemo's and Mylan's ANDAs, which stays are expected to remain in effect until April 2021, May 2021, June 2021 and August 2021, respectively, absent an earlier judgment by the court in each of these lawsuits finding the patents at issue invalid, unenforceable or not infringed. We and the other plaintiffs in each of these lawsuits are seeking, among other relief, an order that the effective date of FDA approval of the ANDA be a date no earlier than the expiration of each of the patents at issue and equitable relief enjoining the Lupin Defendants, the Teva Defendants, the Chemo Defendants and Mylan from infringing these patents.

Opposition Proceedings Against Patents Covering Auryxia

On November 25, 2015, a third party filed an opposition to our issued European Patent No. 1 931 689, or the '689 EP Patent, in the European Patent Office, or the EPO. During the oral proceedings, which took place on June 27, 2017, the Opposition Division of the EPO revoked the '689 EP Patent. On December 6, 2017, we filed an appeal of the decision of the Opposition Division of the EPO, which is presently pending. According to European practice, the revocation of the patent is stayed until an appeal is finally resolved. We anticipate the appeal will take a few years to resolve, during which time the patent will remain in force.

On December 23, 2016, a third party filed an opposition to our issued European Patent No. 1 978 807, or the ’807 EP Patent, in the EPO. During the oral proceedings, which took place on June 8, 2018, the Opposition Division of the EPO maintained the ’807 EP Patent as granted. This decision resulted in the maintenance of all of the claims of the patent, including claims directed to the use of ferric citrate for preventing, reversing, maintaining or delaying progression of chronic kidney disease. On November 16, 2018, the third party filed an appeal of the decision of the Opposition Division of the EPO, which is presently pending. We anticipate the appeal will take a few years to resolve.

Legal Proceedings Relating to Vadadustat

Opposition Proceedings Against Patents Covering Vadadustat

In July 2011, a third party filed an opposition to our issued European Patent No. 2044005, or the ’005 EP Patent, in the EPO. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the EPO maintained the ’005 EP Patent. This decision resulted in the maintenance of a claim directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases, including, but not limited to, anemia. Both parties appealed the decision of the Opposition Division of the EPO. On February 27, 2018, we withdrew the ’005 EP Patent from appeal and filed a divisional patent application to pursue a focused claim set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia.

In September 2018, Dr. Reddy’s Laboratories Limited filed an opposition to our issued Indian Patent No. 287720, or the ’720 IN Patent, in the Indian Patent Office.

Opposition and Invalidity Proceedings Against FibroGen, Inc.

We filed an opposition in the EPO against FibroGen, Inc.’s, or FibroGen’s, European Patent No. 1463823, or the ’823 EP Patent on December 5, 2013, and an oral proceeding took place March 8 and 9, 2016. Following the oral proceeding, the Opposition Division of EPO ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen has appealed that decision. Likewise, we also filed an invalidity proceeding before the Japan Patent Office, or JPO, on June 2, 2014 against certain claims of FibroGen’s Japanese Patent No. 4804131, or the ’131 JP Patent, which is the Japanese counterpart to the ’823 EP Patent, and the JPO issued a preliminary decision finding all of the challenged claims to be invalid. FibroGen subsequently amended the claims and the JPO accepted the amendments. The resulting ’131 JP Patent does not cover vadadustat or any pyridine carboxamide compounds. To date, FibroGen has been unsuccessful in its attempts to obtain a patent in the United States covering the same claim scope as it obtained initially in Europe and Japan in the ’823 EP Patent and ’131 JP Patent. In the event FibroGen were to obtain such a patent in the United States, we may decide to challenge the patent as we have done in Europe and Japan.

On May 13, 2015, May 20, 2015 and July 6, 2015, we filed oppositions to FibroGen’s European Patent Nos. 2322155, or the ’155 EP Patent, 1633333, or the ’333 EP Patent, and 2322153, or the ’153 EP Patent in the EPO, respectively, requesting the patents be revoked in their entirety. These related patents claim, among other things, various compounds that either stabilize HIF or inhibit a HIF hydroxylase or a HIF prolyl hydroxylase, or HIF-PH, for treating or preventing various conditions, including, among other things, iron deficiency, microcytosis associated with iron deficiency, anemia of chronic disease, anemia wherein the subject has a transferrin saturation of less than 20%, anemia refractory to treatment with exogenously administered erythropoietin and microcytosis in microcytic anemia.

Such method of use patents do not prevent persons from using the compound for other uses, including any previously known use of the compound. In particular, these patents do not claim methods of using any of our product candidates for purposes of inhibiting HIF-PH for the treatment of anemia due to chronic kidney disease, or CKD. While we do not believe these patents will prevent us from commercializing vadadustat for the treatment of anemia due to CKD, we filed these oppositions to provide us and our collaborators with maximum flexibility for developing vadadustat and our pipeline of HIF-PHI compounds.

Oppositions to the ’155 EP Patent and the ’153 EP Patent were also filed in the EPO by Glaxo Group Limited, or Glaxo, and by Bayer Intellectual Property GmbH, Bayer Pharma Aktiengesellschaft, and Bayer Animal Health GmbH, or, collectively Bayer.

With regard to the opposition that we filed in Europe against the ’333 EP Patent, an oral proceeding took place on December 8 and 9, 2016. Following the oral proceeding, the Opposition Division of the EPO ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. On December 9, 2016, FibroGen filed a notice to appeal the decision to revoke the ’333 EP Patent.

In oral proceedings held on May 29, 2017, regarding the ’155 EP Patent, the European Opposition Division ruled that the ’155 EP Patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen filed a notice to appeal the decision to revoke the ’155 EP Patent on May 29, 2017.

Subsequently, in related oral proceedings held on May 31, 2017 and June 1, 2017 for the ’153 EP Patent, the Opposition Division of the EPO maintained the patent after FibroGen significantly narrowed the claims to an indication for which vadadustat is not intended to be developed. We and Glaxo separately filed notices to appeal the decision to maintain the ’153 EP Patent on November 9, 2017. Bayer filed a notice to appeal the decision on November 14, 2017.

On May 21, 2018, we filed a Statement of Claim in Canadian Federal Court to challenge the validity of three of FibroGen’s HIF-related patents in Canada: CA 2467689, CA 2468083, and CA 2526496.

On June 22, 2018, we and our collaboration partner in Japan, Mitsubishi Tanabe Pharma Corporation, or MTPC, jointly filed a Request for Trial before the JPO to challenge the validity of one of FibroGen’s HIF-related patents in Japan, JP4845728. On July 20, 2018 and August 13, 2018, we and MTPC jointly filed a Request for Trial before the JPO to challenge the validity of two additional FibroGen HIF-related patents in Japan, JP5474872 and JP5474741, respectively.

On December 13, 2018, we and our collaboration partner, Otsuka Pharmaceutical Company Limited, filed Particulars of Claim in the Patents Court of the United Kingdom, or the UK, to challenge the validity of FibroGen, Inc.’s six HIF-related patents in the UK: the ’823 EP Patent (UK), the ’333 EP Patent (UK), the ’153 EP Patent (UK), the ’155 EP Patent (UK), European Patent (UK) No. 2,289,531, or the ’531 EP Patent (UK), and European Patent (UK) No. 2,298,301, or the ’301 EP Patent (UK). On December 21, 2018, GlaxoSmithKline UK Limited and GlaxoSmithKline Intellectual Property (No. 2) Limited, or collectively Glaxo UK, also filed Particulars of Claim in the Patents Court of the United Kingdom to challenge the validity of the ’153 EP Patent (UK) and the ’155 EP Patent (UK).

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information

Our common stock is traded on The Nasdaq Global Market under the symbol "AKBA".

Holders

At March 1, 2019, there were approximately 24 holders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have never declared or paid any cash dividends on our common stock. We currently intend to retain earnings, if any, for use in our business and do not anticipate paying cash dividends on our common stock in the foreseeable future. Payment of future dividends, if any, on our common stock will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, anticipated cash needs, and plans for expansion.

Issuer Purchases of Equity Securities

None.

Comparative Stock Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or "filed" with the SEC or subject to Regulation 14A or 14C, or to the liabilities of Section 18 of the Exchange Act, except to the extent that we specifically request that this information be treated as soliciting material or we specifically incorporate it by reference into a filing under the Securities Act of 1933, as amended, or the Exchange Act.

Set forth below is a graph comparing the total cumulative returns of Akebia Therapeutics, Inc., the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes $100 was invested on March 20, 2014 in our common stock and each of the indices and that all dividends, if any, are reinvested. The performance shown represents past performance and should not be considered an indication of future performance.

Equity Compensation Plan Information

Information required by Part II, Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchasers of Equity Securities regarding our equity compensation plans is incorporated herein by reference to Part III, Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Item 6. Selected Financial Data

The selected consolidated financial data set forth below for the years ended December 31, 2018, 2017 and 2016 and as of December 31, 2018 and 2017 are derived from our audited consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data for the years ended December 31, 2015 and 2014 and as of December 31, 2016, 2015 and 2014 are derived from our audited consolidated financial statements that are not included elsewhere in this Annual Report on Form 10-K. You should read these data together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K under the captions "Financial Statements and Supplementary Data." The selected financial data in this section are not intended to replace our consolidated financial statements and related notes and are qualified in their entirety by the consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

| | Year Ended December 31, | | | | |
|---|---|---|---|---|---|
| | 2018 | 2017 (as revised) [2] | 2016 | 2015 | 2014 |
| | (in thousands, except share and per share data) | | | | |
| Consolidated statements of operations data: | | | | | |
| Revenues: | | | | | |
| Product revenue, net | $6,824 | $— | $— | $— | $— |
| License, collaboration and other revenue | 200,918 | 181,227 | 1,535 | — | — |
| Total revenues | 207,742 | 181,227 | 1,535 | — | — |
| | | | | | |
| Cost of goods sold | 7,768 | — | — | — | — |
| Operating expenses | 378,135 | 257,901 | 137,995 | 61,513 | 37,940 |
| Loss from operations | (178,161) | (76,674) | (136,460) | (61,513) | (37,940) |
| Other income, net | 6,235 | 3,003 | 713 | 797 | 906 |
| Benefit for income taxes | (28,338) | — | — | — | — |
| Net loss | $(143,588) | $(73,671) | $(135,747) | $(60,716) | $(37,034) |
| Accretion on preferred stock | — | — | — | — | (86,899) |
| Net loss applicable to common shareholders | $(143,588) | $(73,671) | $(135,747) | $(60,716) | $(123,933) |
| Net loss per share applicable to common stockholders— | | | | | |
| basic and diluted[1] | $(2.47) | $(1.69) | $(3.60) | $(2.29) | $(8.04) |
| Weighted-average number of common shares used in | | | | | |
| net loss per share applicable to common stockholders— | | | | | |
| basic and diluted | 58,038,252 | 43,500,795 | 37,716,949 | 26,469,170 | 15,406,386 |

(1) See Note 2 of the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a description of the method used to calculate basic and diluted net loss per share of common stock.

(2) Revenue amount for the year ended December 31, 2017 has been revised to reflect the adoption of ASC 606, with full retrospective application.

| | December 31, | | | | |
|---|---|---|---|---|---|
| | 2018 | 2017 | 2016 | 2015 | 2014 |
| | (in thousands) | | | | |
| Consolidated Balance Sheet Data: | | | | | |
| Cash and cash equivalents and available for sale securities | $321,640 | $317,792 | $260,343 | $138,454 | $108,918 |
| Working capital | 202,582 | 217,250 | 182,053 | 129,149 | 103,595 |
| Total assets | 996,540 | 364,247 | 300,216 | 142,940 | 110,995 |
| Accumulated deficit | (514,395) | (370,807) | (297,136) | (161,389) | (100,673) |
| Total stockholders' equity | 635,928 | 122,574 | 68,120 | 130,998 | 104,078 |

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve significant risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. Please also refer to the section under the heading "Note Regarding Forward-Looking Statements."

Operating Overview

We are a biopharmaceutical company focused on the development and commercialization of therapeutics for patients with kidney disease. On December 12, 2018, we completed a merger, or the Merger, with Keryx Biopharmaceuticals, Inc., or Keryx, combining a nephrology-focused commercial organization with our robust development organization. Following the Merger, Keryx is our wholly owned subsidiary, and we are integrating our business and Keryx's business with the goal of positioning Akebia to realize the potential growth opportunities and synergies from the Merger.

We now have a commercial product and a late-stage product candidate:

- Auryxia® (ferric citrate) is approved and marketed in the United States for two indications: (1) the control of serum phosphorus levels in adult patients with chronic kidney disease, or CKD, on dialysis, or DD-CKD, or the Hyperphosphatemia Indication, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with CKD not on dialysis, or NDD-CKD, or the IDA Indication. Ferric citrate is also approved and marketed in Japan as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, under the trade name Riona® (ferric citrate hydrate) and approved in the European Union, or the EU, for the control of hyperphosphatemia in adult patients with CKD under the trade name Fexeric® (ferric citrate).
- Vadadustat is an investigational, oral hypoxia-inducible factor prolyl hydroxylase inhibitor, or HIF-PHI, in global Phase 3 development for two indications: (1) anemia due to CKD in adult patients with DD-CKD, and (2) anemia due to CKD in adult patients with NDD-CKD. We believe vadadustat has the potential to set a new oral standard of care for patients with anemia due to CKD, subject to regulatory approval. Vadadustat's proposed mechanism of action is designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with increased production of hypoxia-inducible factor, or HIF, which coordinates the interdependent processes of iron mobilization and stimulates endogenous production of erythropoietin, or EPO, to increase red blood cell, or RBC, production and, ultimately, improve oxygen delivery.

We market Auryxia in the United States with our well-established, nephrology-focused commercial organization. Our Japanese sublicensee, Japan Tobacco, Inc., or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize Riona in Japan. Fexeric is not currently marketed in the EU, and our EU marketing authorization for Fexeric will cease to be valid on December 23, 2019 unless we commence marketing Fexeric in the EU by that date. We are exploring commercialization opportunities with third parties for Fexeric.

We plan to commercialize vadadustat, subject to U.S. Food and Drug Administration, or FDA, approval, in the United States with our commercial organization, while also leveraging our collaboration with Otsuka Pharmaceutical Co. Ltd., or Otsuka, and its U.S. commercial organization. We also granted Otsuka exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. In Japan and certain other countries in Asia, we granted Mitsubishi Tanabe Pharma Corporation, or MTPC, exclusive rights to commercialize vadadustat, subject to marketing approvals. In addition, we granted Vifor (International) Ltd., or Vifor Pharma, an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, which manages

approximately 40% of the dialysis patients in the United States, at its U.S. dialysis clinics, subject to FDA approval of vadadustat, vadadustat's reimbursement under a bundled reimbursement model, and a milestone payment by Vifor Pharma.

Since our incorporation as a Delaware corporation in 2007, we have devoted the largest portion of our resources to our development efforts relating to vadadustat, including preparing for and conducting clinical studies of vadadustat, providing general and administrative support for these operations and protecting our intellectual property. Auryxia is our only product approved for sale and it has generated approximately $6.8 million in revenue from product sales from the closing of the Merger through December 31, 2018. We have funded our operations primarily through equity offerings and strategic collaborations.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $143.6 million, $73.7 million and $135.7 million for the years ended December 31, 2018, 2017 and 2016, respectively. Substantially all of our net losses resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. The amount of our future net losses will depend, in part, on the rate of our future expenditures, and our financial position will depend, in part, on our product revenues from Auryxia and, if approved, vadadustat and our ability to obtain funding through equity or debt financings or strategic collaborations. We expect to continue to incur significant expenses if and as we:

- conduct our development program of vadadustat for the treatment of anemia due to CKD, including $PRO_2TECT$, $INNO_2VATE$, $FO_2RWARD$-2, $TRILO_2GY$-2 and $EXPLO_2RE$, and develop plans for and conduct the preclinical and clinical development of any other potential product candidates;
- continue our commercialization activities for Auryxia and plan for the commercialization of vadadustat, if approved, and any other product candidate;
- continue our Merger-related integration activities;
- seek marketing approvals for our product candidates that successfully complete clinical studies, and maintain marketing approvals for Auryxia and any product candidate for which we obtain marketing approval, including complying with any post-marketing regulatory requirements;
- have our product candidates manufactured for clinical trials and for commercial sale;
- initiate additional preclinical, clinical or other studies for vadadustat and any other product candidates, or any post-marketing approval studies, Phase 4 studies or any other clinical trials for Auryxia and Fexeric;
- seek to discover and develop additional product candidates;
- engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we would market and develop commercial products, or develop other product candidates and technologies;
- make royalty, milestone or other payments under our license agreements and any future in-license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel;
- continue to create additional infrastructure and expend additional resources to support our operations as a public company, including any additional infrastructure and resources necessary to support a transition from our status as an emerging growth company; and
- experience any delays or encounter issues with any of the above.

We have one product approved for commercial sale through the Merger but have not generated, and may not generate, enough product revenue from the sale of Auryxia to realize net profits from product sales. We have no manufacturing facilities, and all of our manufacturing activities are contracted out to third parties. Additionally, we currently utilize CROs to carry out our clinical development activities. If we obtain marketing approval for any of our product candidates, and as we continue to commercialize Auryxia, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. If and until we can generate a sufficient amount of revenue from product sales, we expect to finance future cash needs through public or private equity or debt offerings, payments from our collaborators, strategic transactions, or a combination of these approaches. If we are unable to raise additional capital in sufficient amounts when needed or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates. Any of these events could significantly harm our business, financial condition and prospects.

From inception through December 31, 2018, we raised approximately $468.4 million of net proceeds from the sale of equity including $377.4 million from various underwritten public offerings, $41.0 million from an at-the-market offering, or ATM, pursuant to sales agreements with Cantor Fitzgerald & Co and $50.0 million from the sale of 3,571,429 shares of common stock to Vifor Pharma. At inception of our collaboration agreements with Otsuka and

MTPC, they committed to approximately $573.0 million or more in cost-share funding, of which we generally continue to receive on a quarterly prepaid basis, and license payments. Of these commitments, we received approximately $272.0 million at the onset of the collaboration agreements.

Business Combination

On December 12, 2018, we completed the Merger. Pursuant to the terms and conditions of the Agreement and Plan of Merger, or the Merger Agreement, each share of Keryx common stock, or Keryx Share, issued and outstanding immediately prior to the effective time of the Merger, the Effective Time, was cancelled and converted into 0.37433, or the Exchange Multiplier, fully paid and non-assessable shares of Akebia common stock, or Akebia Shares. The Merger Agreement also provided that at the Effective Time, each Keryx Share that was subject to an outstanding Keryx restricted share award, to the extent outstanding, other than those Keryx restricted share awards that accelerated or lapsed as a result of the completion of the Merger, converted into a restricted stock unit, or RSU, award of ours covering the number of Akebia Shares determined in accordance with the Exchange Multiplier. In addition, each outstanding and unexercised option to acquire Keryx Shares converted into an option to acquire Akebia Shares, with the number of shares and exercise price adjusted by the Exchange Multiplier.

As part of the purchase price allocation, we identified developed product rights for Auryxia as the primary intangible asset. The fair value of the developed product rights for Auryxia is determined using the multi-period excess earnings method which is a variation of the income approach, and is a valuation technique that provides an estimate of the fair value of an asset based on the principle that the value of an intangible asset is equal to the present value of the incremental after-tax cash flows attributable to the asset, after taking charges for the use of other assets employed by the business. Key estimates and assumptions used in this model are projected net revenues and expenses related to the asset, estimated contributory asset charges, and a risk-adjusted discount rate of 20.0% used to calculate the present value of the future expected cash inflows from the asset. The intangible asset will be amortized over its estimated useful life, which for Auryxia is 9 years.

The calculation of the excess of the purchase price over the estimated fair value of the tangible net assets and intangible asset acquired was recorded as goodwill. The factors contributing to the recognition of the amount of goodwill were based on several strategic and synergistic benefits that were expected to be realized from the Merger. These benefits included the expectation that the combined company would establish itself as a leading renal company with enhanced position and large market opportunity, synergistic utilization of Keryx's commercial organization, and strengthening the combined company's financial profile. For additional information, please refer to Note 3 to our consolidated financial statements contained in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report.

Additionally, in connection with the Merger, Akebia and Keryx entered into a Notes Conversion Agreement with Baupost Group Securities, L.L.C., or Baupost, the holder of approximately $164.75 million of Keryx's Zero Coupon Convertible Senior Notes due 2021, or the Convertible Notes. Pursuant to the terms of the Notes Conversion Agreement, Baupost agreed to convert the Convertible Notes into 35,582,335 Keryx Shares, or the Conversion Shares, in accordance with the terms of the governing indenture, dated May 9, 2018, by and between Keryx and the Bank of New York Mellon Trust Company, N.A., immediately prior to the Effective Time of the Merger, conditioned upon the issuance to Baupost of an additional 4,000,000 Keryx Shares, or the Additional Shares. The Conversion Shares and the Additional Shares were issued prior to the Effective Time and converted to Akebia Shares with the same Exchange Multiplier as other Keryx Shares. The fair value of the Baupost Additional Shares, on an as-converted basis, of $13.4 million has been excluded from the purchase price and recorded within general and administrative expenses in our consolidated financial statements, as the issuance of those shares by Keryx is considered to be a separate transaction under ASC 805, Business Combinations, since it was entered into by or on behalf of the acquirer or primarily for the benefit of the acquirer or the combined entity. On December 12, 2018, we entered into a Registration Rights Agreement with Baupost, which provides customary registration rights for Akebia Shares issued to Baupost upon consummation of the Merger.

Financial Overview

Revenue

As a result of the Merger, we now have one product, Auryxia, approved for commercial sale. To date, our revenues have been derived from collaboration revenues, which include license and milestone payments and cost-sharing revenue, generated through collaboration and license agreements with partners for the development and commercialization of vadadustat and, following the Merger, commercial sales of Auryxia and royalty revenue from sales of Riona in Japan. Cost-sharing revenue represents amounts reimbursed by our collaboration partners for expenses incurred by us for research and development activities and, potentially, co-promotion activities, under our collaboration agreements.

We expect our revenue to continue to be generated primarily from our commercial sales of Auryxia in the U.S., royalty revenue from JT and Torii, and collaborations with Otsuka and MTPC and any other collaborations into which we may enter.

Cost of goods sold

Cost of goods sold includes direct costs to manufacture commercial drug substance and drug product for Auryxia, as well as indirect costs including costs for packaging, shipping, insurance and quality assurance, idle capacity charges, write-offs for inventory that fails to meet specifications or is otherwise no longer suitable for commercial sale, and royalties due to the licensor of Auryxia related to the U.S. product sales recognized during the period.

As a result of the Merger and the application of purchase accounting, costs of goods sold also includes amortization expense associated with the fair value of the developed product rights for Auryxia, which is being amortized over nine years, as well as expense associated with the fair value inventory step-up, which we expect to incur over approximately two years.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

- personnel-related expenses, including salaries, benefits, recruiting fees, travel and stock-based compensation expense of our research and development personnel;
- expenses incurred under agreements with contract research organizations, or CROs, and investigative sites that conduct our clinical studies;
- the cost of acquiring, developing and manufacturing clinical study materials through contract manufacturing organizations, or CMOs;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies; and
- costs associated with preclinical, clinical and regulatory activities.

Research and development costs are expensed as incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We cannot determine with certainty the duration and completion costs of current or future clinical studies of our product candidates or if, when, or to what extent we will generate revenue from the commercialization and sale of any of our product candidates that obtain marketing approval. We may never succeed in achieving marketing approval for any of our product candidates.

The duration, costs and timing of clinical studies and development of our product candidates will depend on a variety of factors including, but not limited to, those described in Part I, Item 1A. Risk Factors. A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA, the European Medicines Agency, or the EMA, or other regulatory authorities were to require us to conduct clinical studies in addition to or different from those that we currently anticipate, or if we experience delays in any of our clinical studies, we could be required to expend significant additional financial resources and time on the completion of clinical development.

From inception through December 31, 2018, we have incurred $753.8 million in research and development expenses. We plan to increase our research and development expenditures for the foreseeable future as we continue the development of vadadustat and any other product candidates. Our current and/or planned research and development activities include the following:

- global development of vadadustat;
- post-marketing clinical trials of Auryxia;
- research and development of compounds in our HIF portfolio; and
- diversification of our pipeline in kidney disease.

Our direct research and development expenses consist principally of external costs, such as fees paid to clinical trial sites, consultants, central laboratories and CROs in connection with our clinical studies, and drug substance and drug product manufacturing for clinical studies.

We currently have four clinical trials to which the majority of our research and development costs are attributable. We have not accumulated and tracked our research and development costs or our personnel and personnel-related costs on a program-by-program basis as our employee and infrastructure resources, and many of our costs, are directed broadly to applicable research endeavors. As a result, we are unable to specify precisely the costs incurred for each of our programs on a program-by-program basis.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses for our commercial personnel, including our field sales force and other commercial support personnel, as well as personnel in executive and other administrative or non-research and development functions. Other selling, general and administrative expenses include facility-related costs, fees for directors, accounting and legal services fees, recruiting fees and expenses associated with obtaining and maintaining patents.

We anticipate that our selling, general and administrative expenses will increase in the future as we increase our headcount to support continued commercialization of Auryxia and continued research and development and potential commercialization of our product candidates. We also anticipate increased expenses related to finance, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and U.S. Securities and Exchange Commission, or SEC, requirements, and our other costs associated with being a public company, particularly as our compliance obligations will increase once we are no longer an “emerging growth company” after December 31, 2019.

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

| | Year ended December 31, 2018 | 2017 (as revised) | Increase (Decrease) |
|---|---|---|---|
| | (In Thousands) | | |
| Revenues: | | | |
| Product revenue, net | $6,824 | $— | $6,824 |
| License, collaboration and other revenue | 200,918 | 181,227 | 19,691 |
| Total revenues | 207,742 | 181,227 | 26,515 |
| Cost of goods sold: | | | |
| Product | 6,251 | — | 6,251 |
| Amortization of intangibles | 1,517 | — | 1,517 |
| Total cost of goods sold | 7,768 | — | 7,768 |
| Operating expenses: | | | |
| Research and development | 291,007 | 230,893 | 60,114 |
| Selling, general and administrative | 87,061 | 27,008 | 60,053 |
| License expense | 67 | — | 67 |
| Total operating expenses | 378,135 | 257,901 | 120,234 |
| Loss from operations | (178,161) | (76,674) | 101,487 |

| | | | |
|---|---|---|---|
| Other income, net | 6,235 | 3,003 | 3,232 |
| Net loss before income taxes | (171,926) | (73,671 ) | 98,255 |
| Benefit for income taxes | (28,338 ) | — | 28,338 |
| Net loss | $(143,588) | $(73,671 ) | $69,917 |

Revenue. Net product revenue is derived from sales of our sole commercial product, Auryxia. We distribute our product principally through a limited number of wholesale distributors as well as certain specialty pharmacy providers. We began recording product revenue on sales of Auryxia in the U.S. on December 12, 2018 following the consummation of the Merger. During the period from December 12, 2018 through December 31, 2018 we recorded approximately $6.8 million of net product revenue. For net product revenue during the period from December 12, 2018 through December 31, 2018, the average net sales price per unit (after accounting for fees, rebates, chargebacks, and other discounts or reserves, or the gross-to-net adjustment) was approximately 40% of the wholesale acquisition cost, or WAC, which is the gross list price at which our direct customers purchase each unit. The gross-to-net adjustment of product revenue during the period from December 12, 2018 through December 31, 2018 was impacted by the limited time period over which product revenue was recognized and we expect the gross-to-net adjustment to be closer to 50% in future periods. This anticipated future gross-to-net adjustment is an estimate and is based on a variety of assumptions, and the actual gross-to-net adjustment going forward may be materially different.

License, collaboration and other revenue was $200.9 million for the year ended December 31, 2018, compared to $181.2 million for the year ended December 31, 2017. We recognized $200.5 million in collaboration revenue for the year ended December 31, 2018 from our cost sharing arrangement under the Otsuka collaboration agreement for the U.S., or the Otsuka U.S. Agreement, the Otsuka collaboration agreement for certain territories outside the U.S., or the Otsuka International Agreement, as well as revenue recognized in connection with our collaboration agreement with MTPC, or the MTPC Agreement. We recognized $181.2 million in collaboration revenue for the year ended December 31, 2017 from our cost sharing arrangement under the Otsuka U.S. Agreement, which commenced in December 2016, the Otsuka International Agreement, which commenced in April 2017, and the MTPC Agreement, for which the revenue recognition criteria, as required under ASC 606, began to be satisfied in the fourth quarter of 2017. The increase in revenue between the two periods was primarily attributable to an additional $52.9 million of revenue recognized under both the Otsuka U.S. Agreement and Otsuka International Agreement, partially offset by a decrease of $33.6 million of revenue recognized in connection with the MTPC Agreement. The remaining variance is primarily due to an increase in license revenue relating to our sublicense agreement with JT and Torii and includes license fees and royalties on net product sales of Riona in Japan. We expect our collaboration revenue to increase in future periods following an increase in the aggregate percentage of the current global development costs Otsuka funds from 52.5% to 80%, which is expected to occur in the second quarter of 2019.

Cost of Goods Sold - Product. Cost of goods sold of $6.3 million during the period from December 12, 2018 through December 31, 2018 consists primarily of costs associated with the manufacturing of Auryxia and a $4.8 million charge related to the fair-value inventory step-up from the application of purchase accounting.

Cost of Goods Sold - Amortization of Intangibles. Amortization of intangibles relates to the acquired developed product rights for Auryxia. This intangible asset is being amortized over its estimated useful life of approximately 9 years using a straight-line method. Amortization of intangibles for the year ended December 31, 2018 was $1.5 million.

Research and Development Expenses. Research and development expenses were $291.0 million for the year ended December 31, 2018, compared to $230.9 million for the year ended December 31, 2017. The increase of $60.1 million was due to the following:

| | (in millions) |
|---|---|
| PRO$_2$TECT and INNO$_2$VATE Phase 3 program | $ 27.9 |
| Manufacture of drug substance and drug product | 16.1 |
| Regulatory activities and other clinical and preclinical activities | 15.2 |
| FO$_2$RWARD-2 and TRILO$_2$GY-2 studies[1] | (2.9) |
| Japan Phase 2 studies | (9.6) |
| Total increase related to the continued development of vadadustat | 46.7 |
| | |
| Headcount, consulting and facilities | 17.1 |
| Other research | 0.8 |
| Janssen license fee | (1.0) |
| Fair value of warrants issued for Janssen license | (3.4) |
| Other | (0.1) |
| Total net increase | $ 60.1 |

(1) Includes costs from the $FO_2$RWARD, $FO_2$RWARD-2, $TRIL_2$OGY, and $TRILO_2$GY-2 studies.

The increase in the costs related to the development of vadadustat is primarily attributable to an increase in external costs related to the continued advancement of the $PRO_2$TECT and $INNO_2$VATE Phase 3 program, including ongoing enrollment, manufacture of drug substance and drug product in support of the global Phase 3 program, and regulatory activities as well as other clinical and preclinical activities. This increase in costs related to the development of vadadustat was partially offset by a decrease in costs related to the $FO_2$RWARD, $TRILO_2$GY, and Japan Phase 2 studies. The increase in research and development expenses were further impacted by increases in headcount and consulting costs to support our expanding research and development programs. We expect to continue to incur significant research and development expenses in future periods in support of our global Phase 3 program and other studies for vadadustat and development of our other product candidates.

Selling, General and Administrative Expenses. Selling, general and administrative expenses were $87.1 million for the year ended December 31, 2018, compared to $27.0 million for the year ended December 31, 2017. The increase of $60.1 million was primarily due to an increase in legal and other professional fees related to the Merger, including $13.4 million attributed to the fair value of the 4,000,000 Additional Shares issued to Baupost, and an increase in costs to support our research and development programs, including headcount and compensation-related costs. Excluding costs incurred related to the Merger, we expect our selling, general and administrative expenses to increase in future periods to support our continued commercialization of Auryxia, and our continued research and development and potential commercialization of vadadustat and other product candidates.

License Expenses. For the year ended December 31, 2018, we recognized approximately $67,000 in license expense related to royalties due to Auryxia relating to sales of Riona in Japan.

Other Income, Net. Other income, net, was $6.2 million for the year ended December 31, 2018, compared to $3.0 million for the year ended December 31, 2017. Other income, net for the year ended December 31, 2018, was primarily comprised of interest income caused by higher average interest rates on our investments during 2018.

Benefit for Income Taxes. Benefit for income taxes was $28.3 million for the year ended December 31, 2018 due to the release of a portion of our valuation allowance as the deferred tax liabilities, or DTLs, recorded as part of purchase accounting will provide a source of income that allowed us to conclude that certain of our deferred tax assets are realizable. The release of valuation allowance creates a tax benefit in the consolidated statement of operations and comprehensive loss.

Comparison of the Years Ended December 31, 2017 and 2016

| | Year ended December 31, | | Increase (Decrease) |
|---|---|---|---|
| | 2017 (as revised) | 2016 | |
| | (In Thousands) | | |
| Collaboration revenue | $181,227 | $ 1,535 | $ 179,692 |
| Operating expenses: | | | |
| Research and development | 230,893 | 115,785 | 115,108 |
| General and administrative | 27,008 | 22,210 | 4,798 |
| Total operating expenses | 257,901 | 137,995 | 119,906 |
| Loss from operations | (76,674) | (136,460) | 59,786 |
| Other income, net | 3,003 | 713 | 2,290 |
| Net loss | $(73,671) | $ (135,747) | $ 62,076 |

Collaboration Revenue. Collaboration revenue was $181.2 million for the year ended December 31, 2017, compared to $1.5 million for the year ended December 31, 2016. We recognized $1.5 million in collaboration revenue for the year ended December 31, 2016 from our cost sharing arrangement under the Otsuka U.S. Agreement, which commenced in December 2016, and no collaboration revenue from MTPC as the revenue recognition criteria for the MTPC Agreement, as required under ASC 605, had not yet been satisfied. The increase in revenue between the two periods was attributable to an additional $136.7 million of revenue recognized under both the Otsuka U.S. Agreement and Otsuka International Agreement which was consummated in April 2017, as well as $42.9 million of revenue recognized in connection with the MTPC agreement as the revenue recognition criteria as required under ASC 606 was satisfied in the fourth quarter of 2017.

Research and Development Expenses. Research and development expenses were $230.9 million for the year ended December 31, 2017, compared to $115.8 million for the year ended December 31, 2016. The increase of $115.1 million was due to the following:

| | (in millions) |
|---|---|
| PRO$_2$TECT and INNO$_2$VATE Phase 3 program | $ 85.8 |
| FO$_2$RWARD and TRILO$_2$GY studies | 6.3 |
| Japan Phase 2 studies | 5.7 |
| Regulatory activities and other clinical and preclinical activities | 3.0 |
| Manufacture of drug substance | 0.5 |
| Total increase related to the continued development of vadadustat | 101.3 |
| | |
| Headcount, consulting and facilities | 8.2 |
| Fair value of warrants issued for Janssen license | 3.4 |
| Janssen license fee | 1.1 |
| Other | 1.1 |
| Total net increase | $ 115.1 |

The increase in the costs related to the development of vadadustat is primarily attributable to an increase in external costs related to the continued advancement of the PRO$_2$TECT and INNO$_2$VATE Phase 3 program, including ongoing enrollment, the Phase 2 studies in Japan, and study commencement activities for the FO$_2$RWARD and TRILO$_2$GY studies, both of which have been replaced with new study designs. We incurred a total of approximately $20.5 million for the Phase 2 studies in Japan of which MTPC has already paid $20.0 million prior to December 31, 2017, and MTPC will reimburse us for the remaining costs once incurred. The increase in headcount, consulting and facility related costs relates to additional resources required to support our expanding research and development programs.

General and Administrative Expenses. General and administrative expenses were $27.0 million for the year ended December 31, 2017, compared to $22.2 million for the year ended December 31, 2016. The increase of $4.8 million was primarily due to an increase in costs to support our research and development programs, including headcount and compensation-related costs and associated facility-related costs.

Other Income, Net. Other income, net, was $3.0 million for the year ended December 31, 2017, compared to $0.7 million for the year ended December 31, 2016. Other income, net for the year ended December 31, 2017, was primarily comprised of interest income caused by higher average investment balances during 2017. Other income, net for the year ended December 31, 2016 consisted of interest income of $0.9 million offset by expenses related to the write-off of capitalized software.

Liquidity and Capital Resources

We have incurred losses and cumulative negative cash flows from operations since our inception in February 2007, and as of December 31, 2018, we had an accumulated deficit of $514.4 million. We anticipate that we will continue to incur losses for the foreseeable future. We expect that our research and development and selling, general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may raise through a combination of equity offerings, debt financings, other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements.

We have funded our operations principally through sales of our common stock, payments received from our collaboration partners, and following the Merger, product sales. As of December 31, 2018, we had cash and cash equivalents and available for sale securities of approximately $321.6 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Accordingly, available for sale securities, consisting principally of corporate and government debt securities stated at fair value, are also available as a source of liquidity.

Cash Flows

The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

| | Year ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| | (In Thousands) | | |
| Net cash provided by (used in): | | | |
| Operating activities | $(97,494) | $(56,159) | $57,906 |
| Investing activities | 36,594 | (177,260) | 12,705 |
| Financing activities | 96,562 | 116,240 | 66,946 |
| Net increase/(decrease) in cash, cash equivalents and | $35,662 | $(117,179) | $137,557 |

restricted cash

Operating Activities. The cash provided by or used in operating activities in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in the components of working capital. The net cash used in operating activities during the year ended December 31, 2018 of $97.5 million was largely driven by our Phase 3 development program for vadadustat, partially offset by receipt of cash from collaboration agreements. The net cash used by operating activities during the year ended December 31, 2017 of $56.2 million was largely driven by our Phase 3 development program for vadadustat, partially offset by receipt of cash from collaboration agreements, including a $73.0 million up-front payment under the Otsuka International Agreement. The net cash provided by operating activities during the year ended December 31, 2016 of $57.9 million was primarily the result of cash received from collaboration agreements, including $158.8 million received at inception from the Otsuka U.S. Agreement, partially offset by our Phase 3 development program for vadadustat.

Investing Activities. During the year ended December 31, 2018, the net cash provided by investing activities of $36.6 million was comprised primarily from the sale and maturities of available for sale securities, partially offset by purchases of available for sale securities, purchases of equipment and acquisition of the business, net of cash acquired. The net cash used by investing activities during the year ended December 31, 2017 of $177.3 million was comprised primarily from the purchases of available for sale securities of $330.6 million, partially offset by sale of and maturities of available for sale securities and purchases of equipment. Net cash provided by investing activities during the year ended December 31, 2016 of $12.7 million was comprised primarily from the maturities of available for sale securities, partially offset by purchases in available for sale securities and purchases of equipment.

Financing Activities. During the years ended December 31, 2018, 2017 and 2016 our net cash provided by financing activities was $96.6 million, $116.2 million and $66.9 million, respectively. Net cash provided by financing activities for the years ended December 31, 2018, 2017 and 2016 consisted primarily of net proceeds from the public issuance of common stock, proceeds from the exercise of stock options and proceeds from the sale of stock under our employee stock purchase plan.

Operating Capital Requirements

As a result of the Merger, we have one product, Auryxia, approved for commercial sale, but have not generated profits from Auryxia, and may not generate profits from product sales. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek marketing approvals for, our product candidates. We are subject to all risks incident to the development and commercialization of novel therapeutics, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We expect to continue to incur additional costs associated with operating as a public company and we anticipate that we will need substantial additional funding in connection with our continuing operations.

We ended 2018 with cash, cash equivalents and available for sale securities of $321.6 million. At the inception of our collaboration agreements with Otsuka and MTPC, they committed to approximately $573.0 million or more in cost-share funding, of which we generally continue to receive on a quarterly prepaid basis, and royalty and license payments. Of these commitments, we received approximately $272.0 million at the onset of the collaboration agreements. We expect our cash resources, including committed research and development funding from our collaborators, to fund our current operating plan into the third quarter of 2020.

We will require additional capital for the further commercialization of Auryxia, development and potential commercialization of our existing product candidates and will need to raise additional funds sooner to pursue development activities related to additional product candidates. If and until we can generate a sufficient amount of product revenue, we expect to finance future cash needs through public or private equity or debt offerings, payments from our collaborators, strategic transactions, or a combination of these approaches. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Furthermore, our development and regulatory milestones may not be achieved, we may not receive the anticipated funding from our collaboration partners, and we may not secure other sources of financing. Additional funds may not be available to us on acceptable terms or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the commercialization of our product or the development or commercialization of one or more of our product candidates. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders or increased fixed payment obligations, and any such securities may have rights senior to those of our common stock. Any of these events could significantly harm our business, financial condition and prospects.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors. We have based this estimate on assumptions that may be substantially different than actual results, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements, both near- and long-term, will depend on many factors including, but not limited to, those described under Part I, Item 1A. Risk Factors.

If we cannot expand our operations or otherwise capitalize on our business opportunities because we lack sufficient capital, our business, financial condition and results of operations could be materially adversely affected.

Contractual Obligations and Commitments

At December 31, 2018, our future contractual obligations are as follows:

| Payments due by period (in thousands) | Total | Less than 1 year | 1-3 years | 3-5 years | More than 5 years |
|---|---|---|---|---|---|
| Operating Lease Obligations | $46,865 | $6,777 | $14,072 | $12,082 | $13,934 |
| Manufacturing Agreements | 239,068 | 44,685 | 98,192 | 46,691 | 49,500 |
| Debt Obligations | 15,000 | 15,000 | — | — | — |
| Total | $300,933 | $66,462 | $112,264 | $58,773 | $63,434 |

Leases

We lease approximately 65,167 square feet of office and lab space in Cambridge, Massachusetts under a lease which was most recently amended in April 2018, collectively the Cambridge Lease. Under the Third Amendment to the Cambridge Lease, or the Third Amendment, executed in July 2016, total monthly lease payments under the initial base rent were approximately $242,000 and are subject to annual rent escalations. In addition to such annual rent escalations, base rent payments for a portion of said premises commenced on January 1, 2017 in the monthly amount of approximately $22,000. The Fourth Amendment to the Cambridge Lease, executed in May 2017, provided additional storage space to us and did not impact rent payments. In April 2018, we entered into a Fifth Amendment to the Cambridge Lease, or the Fifth Amendment, for an additional 19,805 square feet of office space on the 12th floor. Monthly lease payments for the existing 45,362 square feet of office and lab space, under the Third Amendment, remain unchanged. The new space leased by us was delivered in September 2018 and additional monthly lease payments of approximately $135,000 commenced in February 2019 and are subject to annual rent escalations, commencing in September 2019.

Additionally, as a result of the Merger, we have a lease for 27,300 square feet of office space in Boston, Massachusetts, or the Boston Lease, which expires in February 2023. The total monthly lease payments under the base rent are approximately $136,000 and are subject to annual rent escalations. By the end of 2019, we plan to move employees based in our Boston office to our Cambridge office and sublet our Boston office.

Debt

Keryx, our wholly owned subsidiary following the Merger, has a $40.0 million revolving line of credit, or the Line of Credit, under its Loan and Security Agreement with Silicon Valley Bank, or SVB. Availability under the Line of Credit is subject to a borrowing base comprised of eligible receivables and eligible inventory as set forth in the Loan and Security Agreement. As of December 31, 2018, we had approximately $16.0 million in available borrowing base under the Revolving Loan Facility, of which $15.0 million is outstanding. Proceeds from the Line of Credit may be used for working capital and general business purposes. The Line of Credit is secured by substantially all of Keryx's assets other than intellectual property. The Line of Credit restricts Keryx's ability to grant any interest in its intellectual property other than certain permitted licenses and permitted encumbrances set forth in the Loan and Security Agreement.

The principal amount outstanding under the revolving line bears interest at a floating rate per annum equal to the greater of (i) 2.0% above the "prime rate," as reported in The Wall Street Journal and (ii) 6.75%, which interest is payable monthly. Principal amounts borrowed under the Line of Credit may be repaid and, prior to the maturity date, re-borrowed, subject to the terms and conditions set forth in the Loan and Security Agreement. The Line of Credit will mature on the date that is the earlier of (i) two years after the effective date of the Loan and Security Agreement and (ii) ninety days prior to the maturity of any portion of any Permitted Convertible Debt, as defined under the Loan and Security Agreement. Upon entry into the Loan and Security Agreement (payable in installments and subject to certain conditions), Keryx paid to SVB an initial commitment fee of $149,000, upon the consummation of the Merger, we paid to SVB an additional commitment fee of approximately $251,000, and at the one year anniversary of the effective date of the Loan and Security Agreement(or, if earlier, upon termination of or an event of default under the Loan and Security Agreement), Keryx must pay to SVB a fee equal to 1.00% of the Line of Credit. Keryx is also required to pay on a quarterly basis a fee equal to 0.25% per annum of the average unused portion of the revolving line. Keryx must pay a termination fee of 2.00% of the Line of Credit, if the revolving line is terminated prior to the maturity date, subject to certain exceptions.

The Loan and Security Agreement contains customary covenants applicable to Keryx and its subsidiaries, including maintaining insurance on Keryx's business, achievement of minimum revenue amounts, the incurrence of additional indebtedness, and future encumbrances on the Keryx's assets. In addition, Keryx must maintain a liquidity ratio, defined as (i) the sum of unrestricted and unencumbered cash and cash equivalents maintained at SVB or its affiliates plus net billed accounts receivable divided by (ii) all Keryx's outstanding obligations and liabilities to SVB, including the aggregate amount of our obligations to SVB under any business credit cards, of at least 1.5 to 1.0, measured monthly.

Upon an event of default under the Loan and Security Agreement, SVB is entitled to accelerate and demand payment of all amounts outstanding under the Loan and Security Agreement, stop advancing money or extending credit to Keryx, demand that Keryx deposit at least 105% of the face amount of any letters of credit remaining undrawn to secure all obligations thereunder, and exercise other remedies available to SVB under the Loan and Security Agreement and at law or in equity. As of December 31, 2018, the Company has determined that events of default have already occurred, and has not obtained a formal waiver from SVB with respect to these events of default. As a result, the Company has classified the outstanding principal of $15.0 million as a current liability in its consolidated balance sheet as of December 31, 2018. So long as these events of default are not waived or otherwise resolved, SVB has the right to take any of the foregoing remedies. If SVB were to accelerate all of the obligations outstanding under the Loan and Security Agreement, the Company would be required to pay the outstanding principal and other fees to SVB, and the Company would no longer have access to the Line of Credit. The Company expects its cash resources to fund its current operating plan into the third quarter of 2020, which assumes the payment of all amounts due to SVB and no future borrowings under the Line of Credit.

Manufacturing Agreements

As a result of the Merger, our contractual obligations now include Keryx's commercial supply agreements with BioVectra Inc., or BioVectra, and Siegfried Evionnaz SA, or Siegfried, to supply commercial drug substance for Auryxia.

Pursuant to the BioVectra Manufacture and Supply Agreement and the Product Manufacture and Supply and Facility Construction Agreement, collectively the BioVectra Agreement, we have agreed to purchase a minimum quantity of drug substance of Auryxia at predetermined prices. The price per metric kilogram will decrease with an increase in quantity above the minimum purchase quantity. In addition, the BioVectra Agreement contained contingent milestone payments for capital developments in connection with construction of an expansion of the site of the BioVectra production facility for the manufacture of drug substance for Auryxia. These milestone payments were achieved by BioVectra and paid and fully recorded prior to the Merger. The term of the BioVectra Agreement expires in late 2026, after which, it automatically renews for specified terms until terminated. We have the right to terminate the BioVectra Agreement prior to the contract term, which could result in an early termination fee. As of December 31, 2018, we are required to purchase a minimum quantity of drug substance for Auryxia annually at a total cost of approximately $154.0 million through the year ended December 31, 2026.

As part of purchase accounting, we identified an executory contract in the supply agreement between Keryx and BioVectra, which includes future firm purchase commitments. This executory contract was deemed to have an off-market element related to the amount of purchase commitments that exceed the current forecast and as such, we recorded a liability in purchase accounting. As of the acquisition date, the preliminary fair value of the off-market element was $29.5 million.

Pursuant to the Siegfried Master Manufacturing Services and Supply Agreement, or the Siegfried Agreement, we have agreed to purchase a minimum quantity of drug substance of Auryxia at predetermined prices. The price per metric kilogram will decrease with an increase in quantity above the minimum purchase quantity. The term of the Siegfried Agreement expires on December 31, 2021, after which, it automatically renews for one-year terms until terminated. The Siegfried Agreement provides us with certain termination rights prior to December 31, 2021. As of December 31, 2018, we are required to purchase a minimum quantity of drug substance for Auryxia annually at a total cost of approximately $85.1 million through the year ended December 31, 2021.

Other Third Party Contracts

Under our agreement with IQVIA, formerly known as Quintiles IMS, to provide contract research organization services for the $PRO_2TECT$ and $INNO_2VATE$ programs, the total remaining contract costs as of December 31, 2018 were approximately $106.3 million. The estimated period of performance for the committed work with IQVIA is through the end of 2020. We also contract with various other organizations to conduct research and development activities with remaining contract costs to us of approximately $102.8 million as of December 31, 2018. The scope of the services under these research and development contracts can be modified and the contracts cancelled by us upon written notice, and therefore not included in the table of contractual obligations and commitments. In some instances, the contracts may be cancelled by the third party upon written notice.

Off-Balance Sheet Arrangements

As of December 31, 2018, we did not have any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to prepaid and accrued research and development expenses and stock-based compensation. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Inventories

We value our inventories at the lower-of-cost or net realizable value. We determine the cost of our inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. Prior to the regulatory approval of our product candidates, we incur expenses for the manufacture of material that could potentially be available to support the commercial launch of our products. Until the first reporting period when regulatory approval has been received or is otherwise considered probable and the future economic benefit is expected to be realized, we record all such costs as research and development expense. Inventory used in clinical trials is also expensed as research and development expense, when selected for such use. Inventory that can be used in either the production of clinical or commercial products is expensed as research and development costs when identified for use in a clinical manufacturing campaign. We classify our inventory costs as long-term, in other assets in our consolidated balance sheets, when we expect to utilize the inventory beyond our normal operating cycle.

We perform an assessment of the recoverability of capitalized inventory during each reporting period, and write down any excess and obsolete inventory to our net realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded as a component of cost of product sales in the consolidated statements of operations and comprehensive loss. The determination of whether inventory costs will be realizable requires the use of estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required. Additionally, our product is subject to strict quality control and monitoring that we perform throughout the manufacturing process. In the event that certain batches or units of product no longer meet quality specifications, we will record a charge to cost of product sales to write-down any unmarketable inventory to its estimated net realizable value. In all cases, product inventory is carried at the lower of cost or its estimated net realizable value.

Revenue

We generate revenues primarily from sales of Auryxia, see Note 3 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data, and from our collaborations with MTPC and Otsuka, see Note 4 to our consolidated financial statements in Part II, Item 8 – Financial Statements and Supplementary Data. We recognize revenue in accordance with ASC 606, which applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, we recognize revenue when our 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 we determine are within the scope of ASC 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) the entity satisfies a performance obligation.

We only apply the five-step model to contracts when it is probable that the entity 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 ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations, and assesses 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.

Product Revenue, Net

We sell Auryxia in the U.S., primarily to wholesale distributors as well as certain specialty pharmacy providers, collectively the Customers. These Customers resell our product to health care providers and patients. In addition to distribution agreements with Customers, we enter into arrangements with health care providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks, and discounts with respect to the purchase of our product.

We recognize revenue on product sales when the Customer obtains control of our product, which occurs at a point in time, typically upon delivery to the Customer. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less.

Reserves for Variable Consideration

Revenue from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and which result from discounts, returns, chargebacks, rebates, co-pay assistance and other allowances that are offered within contracts between us and our Customers, health care providers, payors and other indirect customers relating to our sales of our products. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amount will be credited to the Customer) or a current liability (if the amount is payable to a Customer or a party other than a Customer). When appropriate, these estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the respective underlying contracts.

The amount of variable consideration that is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances: We generally provide Customers with discounts that include incentive fees that are explicitly stated in our contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, we compensate (through trade discounts and allowances) our Customers for sales order management, data, and distribution services. However, we have determined such services received to date are not distinct from our sale of products to the Customer and, therefore, these payments have been recorded as a reduction of revenue within the statement of operations and comprehensive loss through December 31, 2018. We record a corresponding reduction to accounts receivable (if the trade discount and/or allowance will be credited to the Customer) or an increase to accrued expense (if the trade discount and/or allowance is payable to a Customer) on the consolidated balance sheets.

Product Returns: Consistent with industry practice, we generally offer Customers a limited right of return which allows for product return when the product expiry is within an allowable window. This right of return lapses once provided to a patient. We estimate the amount of our product sales that may be returned by our Customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized. We currently estimate product return reserve using available industry data and our own historical sales information, including our visibility into the inventory remaining in the distribution channel.

Provider Chargebacks and Discounts: Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to Customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by Customers, and we generally issue credits for such amounts within a few weeks of the Customer's resale of the product. Reserves for chargebacks consist of credits that we expect to issue for units that remain in the distribution channel at each reporting period end that we expect will be sold to qualified healthcare providers, and chargebacks that Customers have claimed but for which we have not yet issued a credit.

Commercial and Medicare Part D Rebates: We contract with various commercial payor organizations, primarily health insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of our products. We estimate the rebates for commercial and Medicare Part D payors based upon (i) our contracts with the payors and (ii) information obtained from our Customers and other third parties regarding the payor mix for Auryxia. We estimate these rebates and record such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Other Government Rebates: We are subject to discount obligations under state Medicaid programs and other government programs. We estimate Medicaid and other government programs rebates based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the consolidated balance sheets. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

Other Incentives: Other incentives that we offer include voluntary patient assistance programs such as our co-pay assistance program, which are intended to provide financial assistance to qualified commercially insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on actual claims processed during a given period, as well as historical utilization data to estimate the amount we expect to receive associated with product that has been recognized as revenue, but remains in in the distribution channel at the end of each reporting period.

Collaboration Revenues

We enter into out-license and collaboration agreements which are within the scope of ASC 606, under which we license certain rights to our product candidates to third parties. The terms of these arrangements typically include payment to us of one or more of the following: non-refundable, up-front license fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services we provide through our contract manufacturers; and royalties on net sales of licensed products. Each of these payments may result in license, collaboration and other revenue, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under each of our agreements, we implement the five-step model noted above. As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine whether the individual deliverables represent separate performance obligations or as a combined performance obligation, and to determine the stand-alone selling price for each performance obligation identified in the contract. A deliverable represents a separate performance obligation if both of the following criteria are met: (i) the customer can benefit from the good or service either on our own or together with other resources that are readily available to the customer, and (ii) the entity’s promise to transfer the good or service to the customer is separately identifiable from other promises in the contract. We use key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates, and probabilities of technical and regulatory success. With regard to the MTPC and Otsuka collaboration agreements, we recognize revenue related to amounts allocated to the identified performance obligation on a proportional performance basis as the underlying services are performed.

Licenses of Intellectual Property

If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees.

We will evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone Payments

At the inception of each arrangement that includes development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. We evaluate factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to assess the milestone as probable of being achieved. There is considerable judgment involved in determining whether a milestone is probable of being reached at each specific reporting period. Milestone payments that are not within our control or the customer, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenues as, or when, the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we will re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue in the period of adjustment.

Manufacturing Supply Services

Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. We asses if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations. If we are entitled to additional payments when the licensee exercises these options, any additional payments are recorded in license, collaboration and other revenues when the licensee obtains control of the goods, which is upon delivery.

Royalties

We will recognize sales-based royalties, including milestone payments based on the level of sales, at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). We receive royalty payments from JT and Torii, based on net sales of Riona in Japan.

Collaborative Arrangements

We record the elements of our collaboration agreements that represent joint operating activities in accordance with ASC Topic 808, Collaborative Arrangements (ASC 808). Accordingly, the elements of the collaboration agreements that represent activities in which both parties are active participants and to which both parties are exposed to the significant risks and rewards that are dependent on the commercial success of the activities are recorded as collaborative arrangements. We consider the guidance in ASC 606-10-15, Revenue from Contracts with Customers – Scope and Scope Exceptions, in determining the appropriate treatment for the transactions between us and our collaborative partner and the transactions between us and third parties. Generally, the classification of transactions under the collaborative arrangements is determined based on the nature and contractual terms of the arrangement along with the nature of the operations of the participants. Therefore, we recognize our allocation of the shared costs incurred with respect to the jointly conducted medical affairs and commercialization and non-promotional activities under the Otsuka U.S. Agreement as a component of the related expense in the period incurred. During the year ended December 31, 2018, we incurred approximately $1.2 million of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement, as defined below in Note 4 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data, of which approximately $0.5 million are reimbursable by Otsuka and recorded as a reduction to research and development expense. During the year ended December 31, 2018, Otsuka incurred approximately $1.1 million of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement, of which approximately $0.5 million are reimbursable by us and recorded as an increase to research and development expense. To the extent product revenue is generated from the collaboration, we will recognize our share of the net sales on a gross basis if it is deemed to be the principal in the transactions with customers, or on a net basis if it is instead deemed to be the agent in the transactions with customers, consistent with the guidance in ASC 606.

Business Combinations

We account for the acquisition of a business in accordance with ASC Topic 805, Business Combinations, or ASC 805. Amounts paid for each acquisition are allocated to the assets acquired and liabilities assumed based on their fair values at the date of acquisition. We determine the fair value of acquired intangible assets based on detailed valuations that use certain information and assumptions provided by management, which is considered management's best estimate of inputs and assumptions that a market participant would use. We allocate any excess purchase price over the fair value of the net tangible and intangible assets acquired to goodwill.

Under ASC 805, transaction costs are not included as a component of consideration transferred and are expensed as incurred. Additionally, in accordance with ASC 805, a transaction entered into by or on behalf of the acquirer or

primarily for the benefit of the acquirer or the combined entity, rather than primarily for the benefit of the acquiree (before the combination), is treated as separate transaction.

Intangible Assets

We maintain definite-lived intangible asset related to developed product rights for Auryxia and a favorable contract, which were acquired on December 12, 2018 as part of the Merger.

Intangible assets are initially recorded at fair value and stated net of accumulated amortization and impairments. We amortize our intangible assets that have finite lives using either the straight-line method, or if reliably determinable, based on the pattern in which the economic benefit of the asset is expected to be utilized. Amortization for our intangible assets are recorded over their estimated useful lives of 4 - 9 years.

We review intangible assets subject to amortization to determine if any adverse conditions exist or a change in circumstances has occurred that would indicate impairment or a change in the remaining useful life. If an impairment indicator exists, we perform a recoverability test by comparing the sum of the estimated undiscounted cash flows of the intangible asset to its carrying value on the consolidated balance sheet. If the carrying value of the intangible asset exceeds the undiscounted cash flows used in the recoverability test, we will write the carrying value down to the fair value in the period identified. We calculate the fair value of intangible assets as the present value of estimated future cash flows expected to be generated from the intangible asset using a risk-adjusted discount rate. In determining our estimated future cash flows associated with our intangible assets, we use market participant assumptions pursuant to ASC 820.

Goodwill

We allocate any excess purchase price over the fair value of the net tangible and intangible assets acquired in a business combination to goodwill. Goodwill is evaluated for impairment on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist.

We compare the fair value of its reporting unit to our carrying value. If the carrying value of the net assets assigned to the reporting unit exceeds the fair value of our reporting unit, we would record an impairment loss equal to the difference. We operate in one operating segment which we consider to be the only reporting unit.

Recent Accounting Pronouncements

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an “emerging growth company” to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We chose to “opt out” of this provision and, as a result, we comply with new or revised accounting standards as required when they are adopted. This decision to opt out of the extended transition period under the JOBS Act is irrevocable.

For a discussion of recent accounting pronouncements, please refer to New Accounting Pronouncements – Recently Adopted and New Accounting Pronouncements – Not Yet Adopted included within Note 2, Summary of Significant Accounting Policies, to our consolidated financial statements included in this report.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2018 and 2017, we had cash and cash equivalents and available for sale securities of $321.6 million and $317.8 million, respectively, primarily money market mutual funds consisting of U.S. government debt securities, certificates of deposit and corporate debt securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are primarily in short-term securities. Our investments are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

Item 8. Financial Statements and Supplementary Data
Akebia Therapeutics, Inc.

Table of Contents

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of

Akebia Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Akebia Therapeutics, Inc. (the "Company") as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the consolidated financial position of the Company at December 31, 2018 and 2017, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

Adoption of ASU No. 2014-09

As discussed in Note 1 to the consolidated financial statements, the Company changed its method of accounting for revenue in 2017 and 2018 due to the adoption of ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606).

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 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 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 audits 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 audits 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 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. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2013.

Boston, Massachusetts

March 26, 2019

AKEBIA THERAPEUTICS, INC.

Consolidated Balance Sheets

(in thousands, except share and per share data)

| | December 31, 2018 | December 31, 2017 (as revised) |
|---|---|---|
| Assets | | |
| Current assets: | | |
| Cash and cash equivalents | $ 104,644 | $ 70,156 |
| Available for sale securities | 216,996 | 247,636 |
| Inventory | 114,245 | — |
| Accounts receivable | 16,666 | 34,216 |
| Prepaid expenses and other current assets | 15,724 | 6,348 |
| Total current assets | 468,275 | 358,356 |
| Property and equipment, net | 8,023 | 3,617 |
| Goodwill | 55,053 | — |
| Other intangible assets, net | 328,153 | — |
| Other assets | 137,036 | 2,274 |
| Total assets | $ 996,540 | $ 364,247 |
| Liabilities and stockholders' equity | | |
| Current liabilities: | | |
| Accounts payable | $ 42,796 | $ 6,998 |
| Accrued expenses | 150,917 | 52,441 |
| Debt | 15,000 | — |
| Short-term deferred revenue | 56,980 | 81,667 |
| Total current liabilities | 265,693 | 141,106 |
| Deferred rent, net of current portion | 3,006 | 2,588 |
| Deferred revenue, net of current portion | 55,709 | 97,957 |
| Deferred tax liabilities | 6,631 | — |
| Other non-current liabilities | 29,573 | 22 |
| Total liabilities | 360,612 | 241,673 |
| Commitments and contingencies (Note 10) | | |
| Stockholders' equity: | | |
| Preferred stock $0.00001 par value, 25,000,000 shares authorized at December 31, 2018 and 2017; 0 shares issued and outstanding at December 31, 2018 and 2017 | — | — |
| Common stock: $0.00001 par value; 175,000,000 shares authorized at December 31, 2018 and 2017; 116,887,518 and 47,612,619 shares issued and outstanding at December 31, 2018 and 2017, respectively | 1 | — |
| Additional paid-in capital | 1,150,583 | 493,823 |
| Accumulated other comprehensive loss | (261) | (442) |
| Accumulated deficit | (514,395) | (370,807) |

| | | |
|---|---|---|
| Total stockholders' equity | 635,928 | 122,574 |
| Total liabilities and stockholders' equity | $ 996,540 | $ 364,247 |

See accompanying notes to consolidated financial statements.

AKEBIA THERAPEUTICS, INC.

Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except share and per share data)

| | Year Ended December 31, 2018 | 2017 (as revised) | 2016 |
|---|---|---|---|
| Revenues: | | | |
| Product revenue, net | $6,824 | $— | $— |
| License, collaboration and other revenue | 200,918 | 181,227 | 1,535 |
| Total revenues | 207,742 | 181,227 | 1,535 |
| | | | |
| Cost of goods sold: | | | |
| Product | 6,251 | — | — |
| Amortization of intangibles | 1,517 | — | — |
| Total cost of goods sold | 7,768 | — | — |
| | | | |
| Operating expenses: | | | |
| Research and development | 291,007 | 230,893 | 115,785 |
| Selling, general and administrative | 87,061 | 27,008 | 22,210 |
| License expense | 67 | — | — |
| Total operating expenses | 378,135 | 257,901 | 137,995 |
| Operating loss | (178,161) | (76,674) | (136,460) |
| Other income (expense): | | | |
| Interest income | 6,154 | 2,799 | 901 |
| Other income/(expense) | 81 | 204 | (188) |
| Net loss before income taxes | (171,926) | (73,671) | (135,747) |
| Benefit for income taxes | (28,338) | — | — |
| Net loss | $(143,588) | $(73,671) | $(135,747) |
| Net loss per share - basic and diluted | $(2.47) | $(1.69) | $(3.60) |
| Weighted-average number of common shares - basic and diluted | 58,038,252 | 43,500,795 | 37,716,949 |
| Comprehensive loss: | | | |
| Net loss | $(143,588) | $(73,671) | $(135,747) |
| Other comprehensive gain (loss) - unrealized gain (loss) on securities | 181 | (400) | (42) |
| Total comprehensive loss | $(143,407) | $(74,071) | $(135,789) |

See accompanying notes to consolidated financial statements.

116

Akebia Therapeutics, Inc.

Consolidated Statements of Stockholders' Equity

(in thousands, except share and per share data)

| | Common Stock $0.00001 Par Value | | Additional Paid-In Capital | Treasury Stock | Unrealized Gain/Loss | Accumulated Deficit | Total Stockholders' Equity |
|---|---|---|---|---|---|---|---|
| | Number of Shares | | | | | | |
| Balance at December 31, 2015 | 30,662,218 | $ — | $292,783 | $ (162) | $ (234) | $ (161,389) | $ 130,998 |
| Issuance of common stock, net of issuance costs | 7,865,293 | — | 66,623 | — | — | — | 66,623 |
| Proceeds from sale of stock under employee stock purchase plan | 16,629 | — | 105 | — | — | — | 105 |
| Forfeitures of restricted common stock | (15,056) | — | — | — | — | — | — |
| Exercise of options | 86,625 | — | 124 | — | — | — | 124 |
| Share-based compensation expense | — | — | 5,825 | — | — | — | 5,825 |
| Unrealized gain/loss | — | — | — | — | 192 | — | 192 |
| Treasury shares retired (8,643) | — | — | (162) | 162 | — | — | — |
| Net loss | — | — | — | — | — | (135,747) | (135,747) |
| Balance at December 31, 2016 | 38,615,709 | $ — | $365,298 | $ — | $ (42) | $ (297,136) | $ 68,120 |
| Issuance of common stock, net of issuance costs | 8,672,270 | — | 114,580 | — | — | — | 114,580 |
| Proceeds from sale of stock under employee stock purchase plan | 44,833 | — | 353 | — | — | — | 353 |
| Forfeitures of restricted common stock | (2,406) | — | — | — | — | — | — |
| Exercise of options | 256,213 | — | 1,312 | — | — | — | 1,312 |
| Share-based compensation expense | — | — | 8,867 | — | — | — | 8,867 |
| Restricted stock unit vesting | 26,000 | — | — | — | — | — | — |
| Issuance of common stock warrants | — | — | 3,413 | — | — | — | 3,413 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Unrealized gain/loss | — | — | — | — | (400) | — | (400) |
| Net loss (as revised) | — | — | — | — | — | (73,671) | (73,671) |
| Balance at December 31, 2017 (as revised) | 47,612,619 | $ — | $493,823 | $ — | $ (442) | $ (370,807) | $ 122,574 |
| Keryx Merger | 57,773,090 | 1 | 527,753 | — | — | — | 527,754 |
| Issuance of Baupost Additional Shares | 1,497,320 | — | 13,386 | — | — | — | 13,386 |
| Issuance of common stock excluding Keryx Merger, net of issuance costs | 9,194,306 | — | 95,452 | — | — | — | 95,452 |
| Proceeds from sale of stock under employee stock purchase plan | 48,768 | — | 482 | — | — | — | 482 |
| Exercise of options | 178,382 | — | 647 | — | — | — | 647 |
| Share-based compensation expense | — | — | 19,040 | — | — | — | 19,040 |
| Restricted stock unit vesting | 583,033 | — | — | — | — | — | — |
| Unrealized gain/loss | — | — | — | — | 181 | | 181 |
| Net loss | — | — | — | — | — | (143,588) | (143,588) |
| Balance at December 31, 2018 | 116,887,518 | $ 1 | $1,150,583 | $ — | $ (261) | $ (514,395) | $ 635,928 |

See accompanying notes to consolidated financial statements.

AKEBIA THERAPEUTICS, INC.

Consolidated Statements of Cash Flows

(in thousands)

| | Year ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 (as revised) | 2016 (as revised) |
| Operating activities: | | | |
| Net loss | $(143,588) | $(73,671) | $(135,747) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Depreciation and amortization | 899 | 617 | 296 |
| Amortization of intangibles | 1,522 | — | — |
| Amortization of premium/discount on investments | (1,232) | 610 | 494 |
| Non-cash interest expense | 28 | — | — |
| Non-cash merger expense[1] | 13,386 | — | — |
| Loss on disposal of property and equipment | — | — | 306 |
| Fair value write-up of inventory sold | 4,771 | — | — |
| Stock-based compensation | 19,040 | 8,867 | 5,825 |
| Deferred income taxes | (28,338) | — | — |
| Fair value of warrants issued for license | — | 3,413 | — |
| Changes in operating assets and liabilities: | | | |
| Accounts receivable | 33,384 | (393) | (33,823) |
| Inventory | 26 | — | — |
| Prepaid expenses and other current assets | (977) | (4,193) | 428 |
| Other long-term assets | 903 | (991) | (2) |
| Accounts payable | 13,717 | 4,959 | (274) |
| Accrued expense | 55,482 | 21,974 | 20,703 |
| Deferred revenue | (66,935) | (17,665) | 197,289 |
| Deferred rent | 418 | 314 | 2,411 |
| Net cash provided by (used in) operating activities | (97,494) | (56,159) | 57,906 |
| Investing activities: | | | |
| Acquisition of business, net of acquired cash and restricted cash | 6,147 | — | — |
| Purchase of equipment | (1,606) | (1,622) | (2,662) |
| Proceeds from the maturities of available for sale securities | 243,269 | 149,998 | 162,376 |
| Proceeds from sales of available for sale securities | 13,000 | 5,000 | — |
| Purchase of available for sale securities | (224,216) | (330,636) | (147,009) |
| Net cash provided by (used in) investing activities | 36,594 | (177,260) | 12,705 |
| Financing activities: | | | |
| Proceeds from the issuance of common stock, net of issuance costs | 95,452 | 114,580 | 66,736 |
| Proceeds from the sale of stock under employee stock purchase plan | 482 | 353 | 106 |
| Proceeds from the exercise of stock options | 647 | 1,312 | 124 |
| Payments on capital lease obligations | (19) | (5) | (20) |
| Net cash provided by financing activities | 96,562 | 116,240 | 66,946 |
| Increase (decrease) in cash, cash equivalents, and restricted cash | 35,662 | (117,179) | 137,557 |

| | | | |
|---|---|---|---|
| Cash, cash equivalents, and restricted cash at beginning of the period | 71,437 | 188,616 | 51,059 |
| Cash, cash equivalents, and restricted cash at end of the period | $107,099 | $71,437 | $188,616 |
| Non-cash financing activities | | | |
| Fair value of shares and equity awards issued in acquisition | $527,754 | $— | $— |
| Unpaid follow-on offering costs | $— | $— | $12 |

(1) Relates to non-cash expense associated with the fair value of the Baupost additional shares (see Note 5).

See accompanying notes to consolidated financial statements.

Akebia Therapeutics, Inc.

Notes to Consolidated Financial Statements

1. Nature of Organization and Operations

Akebia Therapeutics, Inc., referred to as Akebia or the Company, was incorporated in the State of Delaware in 2007. Akebia is a biopharmaceutical company focused on the development and commercialization of therapeutics for patients with kidney disease. Akebia's commercial product, Auryxia® (ferric citrate) is currently approved by the United States Food and Drug Administration, or FDA, and marketed for two indications in the United States, the control of serum phosphorus levels in adult patients with chronic kidney disease, or CKD, on dialysis, or DD-CKD, and the treatment of iron deficiency anemia, or IDA, in adult patients with CKD not on dialysis, or NDD-CKD. Ferric citrate is also approved and marketed in Japan as an oral treatment for the improvement of hyperphosphatemia in patients with DD-CKD and NDD-CKD under the trade name Riona® and approved, but not currently marketed, in the European Union as an oral treatment for the control of hyperphosphatemia in adult patients with DD-CKD and NDD-CKD under the trade name Fexeric®. The Company's lead investigational product candidate, vadadustat, is an oral therapy in Phase 3 development. The Company believes vadadustat has the potential to set a new standard of care in the treatment of anemia due to CKD, acting via a novel hypoxia inducible factor, or HIF, pathway. HIF is the primary regulator of the production of red blood cells, or RBCs, in the body, as well as other important metabolic functions.

On December 12, 2018, the Company completed a merger with Keryx Biopharmaceuticals, Inc., or Keryx, or the Merger. Pursuant to the terms and conditions of the Agreement and Plan of Merger, or the Merger Agreement, each share of Keryx common stock, or Keryx Share, issued and outstanding immediately prior to the effective time of the Merger, or the Effective Time, was cancelled and converted into 0.37433, or the Exchange Multiplier, fully paid and non-assessable shares of Akebia common stock, or Akebia Shares, resulting in the issuance of an aggregate of 59,270,410 Akebia Shares. The Merger Agreement also provided that at the Effective Time, each Keryx restricted share award, to the extent outstanding, other than those Keryx restricted share awards that accelerated or lapsed as a result of the completion of the Merger, converted into an Akebia restricted stock unit, or RSU, award covering the number of Akebia Shares determined in accordance with the Exchange Multiplier, resulting in the issuance of Akebia RSUs covering an aggregate of 602,752 Akebia Shares. In addition, each outstanding and unexercised option to acquire Keryx Shares converted into an option to acquire Akebia Shares, with the number of shares and exercise price adjusted by the Exchange Multiplier, resulting in the assumption by Akebia of options to acquire an aggregate 3,967,290 Akebia Shares. Refer to Note 5 for additional details on the Merger.

Since inception, the Company has devoted most of its resources to research and development, including its preclinical and clinical development activities, raising capital, and providing general and administrative support for these operations. The Company began recording revenue from the U.S. sales of Auryxia on December 12, 2018 and revenue from sublicensing rights to Auryxia in Japan to the Company's Japanese partners Japan Tobacco, Inc. and its subsidiary Torii Pharmaceutical Co., Ltd., collectively JT and Torii. Ferric citrate is approved in Japan under the trade name Riona and in Europe under the trade name Fexeric. The Company has not generated a profit to date and may never generate profits from product sales. The Company's product candidates are subject to long development cycles, and the Company may be unsuccessful in its efforts to develop, obtain marketing approval for or market its product candidates.

The Company is subject to a number of risks including, but not limited to, risks relating to integration following the Merger, the need to obtain adequate additional funding, including the resources necessary to fund commercialization of Auryxia, the global Phase 3 program for vadadustat in NDD-CKD, called PRO$_2$TECT, and DD-CKD, called INNO$_2$VATE, and post-approval studies with respect to Auryxia, risks relating to market acceptance, coverage and

reimbursement of Auryxia, risks related to maintaining the Company's commercial organization and capabilities, risks relating to potential generic entrants, risks of clinical trial failures, the risk of relying on third parties, the risk that the Company never achieves profitability, protection of proprietary technology, compliance with governmental regulations, and dependence on key personnel, and the impact of legal, regulatory and administrative proceedings. Overall, the $PRO_2$TECT and $INNO_2$VATE Phase 3 programs are designed to enroll up to approximately 7,600 patients. In August 2016, the first patient was dosed in $INNO_2$VATE. The Company completed enrollment in the larger of the two $INNO_2$VATE studies, which enrolled 3,554 subjects, in February 2019, and it expects to complete enrollment in the smaller $INNO_2$VATE study, enrolling approximately 350 subjects, by April 2019. The Company anticipates completing the larger of the two $INNO_2$VATE studies in the first quarter of 2020, with completion of the smaller $INNO_2$VATE study and availability of top-line data expected in the second quarter of 2020, subject to the accrual of major adverse cardiovascular events, or MACE. The first patient was dosed in $PRO_2$TECT in December 2015. The Company expects full enrollment of $PRO_2$TECT in 2019. The Company anticipates reporting top-line clinical data for the $PRO_2$TECT studies in mid-2020, subject to the accrual of MACE.

In December 2015, the Company entered into a collaboration agreement with Mitsubishi Tanabe Pharma Corporation, or MTPC, to develop and commercialize vadadustat in Japan and certain other countries in Asia, collectively, the MTPC Territory, for total payments of up to $245.0 million, comprised of a $20.0 million upfront payment, up to $50.0 million in specified development and regulatory milestones, and up to $175.0 million in specified commercial milestones, as well as tiered double-digit royalty payments up to 20% on sales of vadadustat in the MTPC Territory, subject to a reduction upon launch of a generic product on a country-by-country basis (Note 4).

In December 2016, the Company entered into a collaboration and license agreement with Otsuka Pharmaceutical Co. Ltd., or Otsuka to develop and commercialize vadadustat in the United States. In December 2016, the Company received $125.0 million upfront payment, and in March 2017, Otsuka reimbursed the Company approximately $33.8 million for global expenses previously incurred by us for its ongoing global development program for vadadustat in DD-CKD and NDD-CKD patients. The agreement also provides for additional funding for the global development program for vadadustat, totaling $167.5 million or more, depending on the actual global development costs incurred. In addition, Akebia is eligible to receive from Otsuka up to $190.0 million in specified development and regulatory milestones and up to $575.0 million in specified commercial milestones. The Company will share with Otsuka the costs of developing and commercializing vadadustat in the United States and the profits from sales of vadadustat in the United after approval by the FDA and commercial launch (Note 4).

In April 2017, the Company entered into a collaboration and license agreement with Otsuka to develop and commercialize vadadustat in Europe, Russia, China, Canada, Australia, the Middle East and certain other territories. In April 2017, the Company received a $73.0 million upfront payment and $0.2 million for global expenses previously incurred by the Company in implementing the current global Phase 3 development plan for vadadustat in DD-CKD and NDD-CKD patients in excess of a specified threshold during the quarter-ended March 31, 2017. The agreement also provides for additional funding for the global development program for vadadustat, totaling $176.1 million or more, depending on the actual global development costs incurred. In addition, Akebia is eligible to receive from Otsuka up to $132.0 million in specified development and regulatory milestones and up to $525.0 million in specified commercial milestones (Note 4).

From inception through December 31, 2018 the Company has raised approximately $468.4 million of net proceeds, including $377.4 million from several underwritten public offerings, $41.0 million from an at-the-market offering, or ATM, pursuant to sales agreements with Cantor Fitzgerald & Co. and $50.0 million from the sale of 3,571,429 shares of common stock to Vifor (International) Ltd., or Vifor Pharma. At inception of the Company’s collaboration agreements with Otsuka and MTPC, they committed to approximately $573.0 million or more in cost-share funding, which the Company generally continues to receive on a quarterly prepaid basis, and license payments. Of these commitments, the Company received approximately $272.0 million at the onset of the collaboration agreements.

Management of the Company completed its going concern assessment in accordance with ASC 205-40. The Company believes that its cash resources will be sufficient to allow the Company to fund its current operating plan through at least the next twelve months from the filing of the Company’s 2018 Annual Report on Form 10-K, as required by ASC 205-40. There can be no assurance, however, that the current operating plan will be achieved in the time frame anticipated by the Company, or that its cash resources will fund the Company’s operating plan for the period anticipated by the Company or that additional funding will be available on terms acceptable to the Company, or at all. The Company will require additional capital for the further commercialization of Auryxia and continued development and potential commercialization of the Company’s existing product candidates and would need to raise additional funds to pursue development activities related to any additional product candidates. If and until the Company can

generate a sufficient amount of product revenue, the Company expects to finance future cash needs through public or private equity or debt offerings, payments from its collaborators, strategic transactions, or a combination of these approaches.

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 balances and transactions have been eliminated in consolidation. These consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (U.S. GAAP). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification (ASC) and Accounting Standards Update (ASU) of the Financial Accounting Standards Board (FASB).

As discussed more fully below, as prescribed by the required adoption of ASC 606 on January 1, 2018, the Company revised its comparative financial statements for the year ended December 31, 2017 to give effect to ASC 606 as if it had been effective for that period. No changes for the adoption of ASC 606 were deemed necessary for the year ended December 31, 2016 and applicable interim periods within the year.

New Accounting Pronouncements – Recently Adopted

In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606), a new revenue recognition standard which amends revenue recognition principles and provides a single, comprehensive set of criteria for revenue recognition within and across all industries. This ASU supersedes the revenue recognition requirements in ASC Topic 605, Revenue Recognition. In 2015 and 2016, the FASB issued additional ASUs related to Topic 606, or ASC 606, that delayed the effective date of the guidance and clarified various aspects of the new revenue guidance, including principal versus agent considerations, identifying performance obligations, and licensing, and they include other improvements and practical expedients. The Company adopted this new standard on January 1, 2018 using the full retrospective transition method, and has elected to use the following practical expedients that are permitted under the rules of the adoption, which have been applied consistently to all contracts within all reporting periods presented:

- For all reporting periods presented before January 1, 2018, the Company has not disclosed the amount of the transaction price allocated to the remaining performance obligations or an explanation of when the Company expects to recognize the amount as revenue.
- The Company has not adjusted the promised amount of consideration for the effects of a significant financing component when the Company expects, at contract inception, that the period between when the entity transfers a promised good or a service to a customer and when the customer pays for that good or service will be one year or less.
- The Company recognizes the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that the Company otherwise would have recognized is one year or less.

As a result of adopting ASC 606 on January 1, 2018, the Company has revised its comparative financial statements for the year ended December 31, 2017 as if ASC 606 had been effective for that period, as set forth below. No changes for the adoption of ASC 606 were deemed necessary for the year ended December 31, 2016 and applicable interim periods within the year.

With respect to the collaboration agreements with Otsuka, the Company concluded that there was no impact to revenue for the year ended December 31, 2017 after the adoption of ASC 606.

The changes shown in the table below relate to the Company's collaboration agreement with MTPC and the impact of when milestone payments can be recognized under the new standard as well as the period over which this revenue is recognized. Under ASC 605-28, Revenue Recognition-Milestone Method, the Company evaluated at contract inception whether each milestone was substantive. Substantive milestones are recognized as revenue in their entirety upon achievement, assuming all other revenue recognition criteria are met. Therefore, a $4.0 million MTPC development milestone, which was deemed to be substantive, would have been recognized in its entirety in the first quarter of 2018, when the milestone event occurred. Under ASC 606, these substantive milestone payments would be classified as variable consideration and included in the allocable transaction price over the remaining period of performance when it is probable that a significant reversal in the cumulative amount of revenue recognized would not occur. Under ASC 606, this resulted in the $4.0 million MTPC development milestone being included in the allocable consideration, of which $3.2 million was recognized as revenue in 2017 under the proportional performance method utilized for revenue recognition of the MTPC allocable consideration. As a result, the following financial statement line items for the year ended December 31, 2017 were affected.

Consolidated Statement of Operations and Comprehensive Loss

| | For the Year Ended December 31, 2017 |
|---|---|

| | (in thousands, except per share data) | | |
|---|---|---|---|
| | As revised under ASC 606 | As originally reported under ASC 605 | Effect of change |
| Collaboration revenue | $181,227 | $177,984 | $3,243 |
| Operating loss | (76,674) | (79,917) | 3,243 |
| Net loss | (73,671) | (76,914) | 3,243 |
| Net loss per share - basic and diluted | $(1.69) | $(1.77) | $0.08 |

Consolidated Balance Sheets

| | December 31, 2017 (in thousands) | | |
|---|---|---|---|
| | As revised under ASC 606 | As originally reported under ASC 605 | Effect of change |
| Short-term deferred revenue | $81,667 | $84,910 | $(3,243) |
| Accumulated deficit | $(370,807) | $(374,050) | $3,243 |

Consolidated Statement of Cash Flows

| | For the Year Ended December 31, 2017 (in thousands) | | |
|---|---|---|---|
| | As revised under ASC 606 | As originally reported under ASC 605 | Effect of change |
| Net loss | $(73,671) | $(76,914) | $3,243 |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Deferred revenue | (17,665) | (14,422) | (3,243) |
| Cash, cash equivalents, and restricted cash at beginning of the period | 188,616 | 188,616 | — |
| Cash, cash equivalents, and restricted cash at end of the period | $71,437 | $71,437 | $— |

In October 2016, the FASB issued ASU 2016-18, Restricted Cash, which requires that a statement of cash flows explain the change during the period in the total of cash, cash equivalents, and amounts generally described as restricted cash or restricted cash equivalents. Therefore, amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 is effective for fiscal years beginning after December 15, 2017 (fiscal year 2018 for the Company), and interim periods within those years, using a retrospective transition method to each period presented, with early adoption permitted. The Company elected to

adopt this ASU effective January 1, 2018. The adoption of this guidance resulted in $1.3 million in restricted cash to be included with cash and cash equivalents at the beginning of the period in the consolidated statement of cash flows for each of the years ended December 31, 2018, 2017 and 2016.

In May 2017, the FASB issued ASU 2017-09, Compensation – Stock Compensation (Topic 718): Scope of Modification Accounting, which provides guidance about which changes to the terms or conditions of a share-based award require an entity to apply modification accounting under ASC 718, Compensation – Stock Compensation. Specifically, awards will require modification accounting if the fair value, vesting condition or classification of the award is not the same immediately before and after a change to the terms and conditions of the award. This ASU is effective on a prospective basis beginning on January 1, 2018, with early adoption permitted. The Company adopted this ASU effective January 1, 2018, and since the Company did not have any modifications in fiscal 2018, the adoption of this ASU did not have an impact on the Company's consolidated financial statements and disclosures.

New Accounting Pronouncements – Not Yet Adopted

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842), which supersedes the existing guidance for lease accounting, Leases (Topic 840). ASU 2016-02 requires entities to recognize right-of-use assets and lease liabilities for leases with lease terms of more than 12 months on their balance sheets and provide enhanced disclosures. In July 2018, the FASB issued additional ASUs related to Topic 842, or ASC 842, that clarified various aspects of the new lease guidance, including how to record certain transition adjustments, as well as other improvements and practical expedients. ASC 842 is effective for fiscal years beginning after December 15, 2018 and interim periods within those fiscal years. Early application is permitted for all entities; however, the Company has elected not to early adopt. ASC 842 requires a modified retrospective approach for all leases existing at, or entered into after, the date of initial application, with an option to elect to use certain transition relief. The Company is currently evaluating the impact of this new standard on its consolidated financial statements and related disclosures; however, it expects the adoption of this new guidance will result in the Company recording additional assets and corresponding liabilities on its consolidated balance sheets, primarily relating to leases of office and lab space. The Company plans to adopt ASC 842 using the modified retrospective approach with the cumulative effect of adoption recognized to retained earnings on January 1, 2019. The Company also expects to elect the practical expedients upon transition that will retain the lease classification and initial direct costs for any leases that existed prior to the adoption of this new standard. The Company will not reassess whether any contracts entered into prior to the adoption are leases. The Company is also in the process of implementing appropriate changes to its controls to support lease accounting and related disclosures under the new standard.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments, which requires that financial assets measured at amortized cost be presented at the net amount expected to be collected. Currently, U.S. GAAP delays recognition of the full amount of credit losses until the loss is probable of occurring. Under this ASU, the income statement will reflect an entity's current estimate of all expected credit losses. The measurement of expected credit losses will be based upon historical experience, current conditions, and reasonable and supportable forecasts that affect the collectability of the reported amount. Credit losses relating to available-for-sale debt securities will be recorded through an allowance for credit losses rather than as a direct write-down of the security. This ASU is effective for annual periods beginning after December 15, 2019, and is applicable to the Company in fiscal year 2020. Early adoption is permitted. The Company is currently evaluating the impact of the adoption of ASU 2016-13 on its consolidated financial position and results of operations.

In January 2017, the FASB issued ASU 2017-04, Intangibles-Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment, which simplifies how companies calculate goodwill impairments by eliminating Step 2 of the impairment test. Step 2 measures a goodwill impairment loss by comparing the implied fair value of a reporting unit's goodwill with the carrying amount of that goodwill. ASU 2017-04 requires companies to compare the fair value of a reporting unit to its carrying amount and recognize an impairment charge for the amount by which the carrying amount exceeds the reporting unit's fair value; however, the loss recognized should not exceed the total amount of goodwill allocated to the related reporting unit. This ASU is effective for annual periods beginning after December 15, 2019, and is applicable to the Company in fiscal year 2020. Early adoption is allowed, and the Company expects to early adopt ASU 2017-04 for annual and interim goodwill impairment tests conducted after January 1, 2019.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the business of developing and commercializing novel therapeutics for patients with kidney disease.

Derivative Financial Instruments

The Company accounts for warrants and other derivative financial instruments as either equity or liabilities in accordance with ASC Topic 815, Derivatives and Hedging, or ASC 815, based upon the characteristics and provisions of each instrument. Warrants classified as equity are recorded at fair value as of the date of issuance on the Company's consolidated balance sheets and no further adjustments to their valuation are made. Warrants classified as derivative liabilities and other derivative financial instruments that require separate accounting as liabilities are recorded on the Company's consolidated balance sheets at their fair value on the date of issuance and will be revalued on each subsequent balance sheet date until such instruments are exercised or expire, with any changes in the fair value between reporting periods recorded as other income or expense. The warrant issued by the Company in connection with the Janssen Pharmaceutica NV Research and License Agreement, the Janssen Agreement, is classified as equity in the Company's consolidated balance sheet. (See Note 12).

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results may differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of

these financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including: expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes, and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: prepaid and accrued research and development expense, stock-based compensation expense, product and collaboration revenues including various rebates and reserves related to product sales, inventories, income taxes, purchase price allocations related to business combinations, intangible assets and goodwill.

Cash and Cash Equivalents

Cash and cash equivalents consist of all cash on hand, deposits and funds invested in available for sale securities with original maturities of three months or less at the time of purchase. Cash equivalents are reported at fair value. At December 31, 2018, the Company’s cash equivalents are primarily in money market funds. The Company may maintain balances with its banks in excess of federally insured limits.

Restricted cash is included in “other assets” in the consolidated balance sheets.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported in the consolidated balance sheet that sum to the total of the amounts reported in the consolidated statement of cash flows subsequent to the adoption of ASU 2016-18 (in thousands):

| | December 31, 2018 | December 31, 2017 | December 31, 2016 | December 31, 2015 |
|---|---|---|---|---|
| Cash and cash equivalents | $ 104,644 | $ 70,156 | $ 187,335 | $ 49,778 |
| Other assets | 2,455 | 1,281 | 1,281 | 1,281 |
| Total cash, cash equivalents, and restricted cash shown in the statement of cash flows | $ 107,099 | $ 71,437 | $ 188,616 | $ 51,059 |

Restricted cash represents amounts required for security deposits under the Company’s office and lab space lease agreements and cash balances held as collateral for the Company’s employee credit card program.

Investments

Management determines the appropriate classification of securities at the time of purchase and reevaluates such designation as of each balance sheet date. Currently, the Company classifies all securities as available for sale which are included in current assets as they are intended to fund current operations. The Company carries available for sale securities at fair value. The Company conducts periodic reviews to identify and evaluate each investment that has an unrealized loss, in accordance with the meaning of other-than-temporary impairment and its application to certain investments. When assessing whether a decline in the fair value of a security is other-than-temporary, the Company considers the fair market value of the security, the duration of the security’s decline, and prospects for the underlying business. Based on these considerations, the Company did not identify any other-than-temporary unrealized losses at December 31, 2018. Unrealized losses on available for sale securities that are determined to be temporary, and not related to credit loss, are recorded in accumulated other comprehensive loss, a component of stockholders’ equity. The amortized cost of debt securities in this category reflects amortization of premiums and accretion of discounts to maturity computed under the effective interest method. The Company includes this amortization in the caption “Interest income” within the consolidated statements of operations and comprehensive loss. The Company also includes in net investment income, realized gains and losses and declines in value determined to be other than temporary. The Company bases the cost of securities sold upon the specific identification method and includes interest and dividends on securities in interest income.

Accounts Receivable

The Company’s accounts receivable represents amounts due to the Company from product sales (see Note 3) and from its collaboration agreements with MTPC and Otsuka (see Note 4). Reimbursable costs that have not been invoiced as of the balance sheet date are recorded as unbilled accounts receivable. Accounts receivable arising from product sales primarily represent amounts due from wholesale distributors as well as certain specialty pharmacy providers, or collectively, Customers. The Company deducts trade allowances for prompt payment, among other discounts, from its accounts receivable based on its experience that the Company’s Customers will earn these discounts and fees.

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices not specifically reviewed as well as historical payment patterns and existing economic factors. The Company believes that credit risks associated with its Customers and collaboration partners are not significant. The Company did not have an allowance for doubtful accounts as of December 31, 2018 and 2017.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Cash, cash equivalents, investments, and accounts receivable are the only financial instruments that potentially subject the Company to concentrations of credit risk. The Company maintains its cash, cash equivalents, and investments with high quality, accredited financial institutions and, accordingly, such funds are subject to minimal credit risk. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

Accounts receivable represent amounts due from the Company's Customers and collaboration partners. As part of its credit management policy, the Company performs ongoing credit evaluations of its Customers and generally does not require collateral from any customer. The Company also monitors economic conditions of its collaboration partners to identify facts or circumstances that may indicate that any of its accounts receivable are at risk of collection.

Gross revenues and accounts receivable from each of the Company's Customers or collaboration partners who individually accounted for 10% or more of total gross revenues and/or 10% or more of total gross accounts receivable consisted of the following:

| | Percent of Total Gross Revenues Years Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 (as revised) | 2016 |
| Otsuka Pharmaceutical Co. Ltd. | 90% | 76 % | 100 % |

| | Percent of Gross Accounts Receivable As of December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Fresenius Medical Care Rx | 42 % | — |
| McKesson Corporation | 22 % | — |
| Cardinal Health, Inc. | 13 % | — |
| AmerisourceBergen Drug Corporation | 11 % | — |
| Otsuka Pharmaceutical Co. Ltd. | — | 96 % |

Property and Equipment

Property and equipment is stated at cost, less accumulated depreciation. Assets under capital lease are included in property and equipment. Property and equipment is depreciated using the straight-line method over the estimated useful lives of the assets, generally three to seven years. Such costs are periodically reviewed for recoverability when impairment indicators are present. Such indicators include, among other factors, operating losses, unused capacity, market value declines and technological obsolescence. Recorded values of asset groups of equipment that are not expected to be recovered through undiscounted future net cash flows are written down to current fair value, which generally is determined from estimated discounted future net cash flows (assets held for use) or net realizable value (assets held for sale).

The following is the summary of property and equipment and related accumulated depreciation as of December 31, 2018 and 2017.

| | Useful Life | December 31, 2018 | December 31, 2017 |
|---|---|---|---|
| | | (in thousands) | |
| Computer equipment and software | 3 | $1,593 | $ 630 |
| Furniture and fixtures | 5-7 | 1,170 | 800 |
| Equipment | 7 | 1,780 | 628 |
| Leasehold improvements | Shorter of the useful life or remaining lease term (10 years) | 5,324 | 2,582 |
| Office equipment under capital lease | 3 | 114 | 36 |
| | | 9,981 | 4,676 |
| Less accumulated depreciation | | (1,958) | (1,059) |
| Net property and equipment | | $8,023 | $ 3,617 |

Depreciation expense, including expense associated with assets under capital leases, was approximately $0.9 million, $0.6 million and $0.3 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Inventories

The Company values its inventories at the lower-of-cost or net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. The Company classifies its inventory costs as long-term, in other assets in its consolidated balance sheets, when it expects to utilize the inventory beyond their normal operating cycle.

Prior to the regulatory approval of its product candidates, the Company incurs expenses for the manufacture of material that could potentially be available to support the commercial launch of its products. Until the first reporting period when regulatory approval has been received or is otherwise considered probable and the future economic benefit is expected to be realized, the Company records all such costs as research and development expense. Inventory used in clinical trials is also expensed as research and development expense, when selected for such use. Inventory that can be used in either the production of clinical or commercial products is expensed as research and development costs when identified for use in a clinical manufacturing campaign.

The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and writes down any excess and obsolete inventory to its net realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded as a component of cost of product sales in the consolidated statements of operations and comprehensive loss. The determination of whether inventory costs will be realizable requires the use of estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required. Additionally, the Company’s product is subject to strict quality control and monitoring that it performs throughout the manufacturing process. In the event that certain batches or units of product no longer meet quality specifications, the Company will record a charge to cost of product sales to write-down any unmarketable inventory to its estimated net realizable value. In all cases, product inventory is carried at the lower of cost or its estimated net realizable value.

Revenue Recognition

The Company generates revenues primarily from sales of Auryxia, see Note 3, and from its collaborations with MTPC and Otsuka, see Note 4. The Company recognizes revenue in accordance with ASC 606, which applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, 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 the Company determines are within the scope of ASC 606, it 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 ASC 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.

Product Revenue, Net

The Company sells Auryxia in the United States, or U.S., primarily to wholesale distributors as well as certain specialty pharmacy providers. These Customers resell the Company's product to health care providers and patients. In addition to distribution agreements with Customers, the Company enters into arrangements with health care providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks, and discounts with respect to the purchase of the Company's product.

The Company recognizes revenue on product sales when the Customer obtains control of the Company's product, which occurs at a point in time, typically upon delivery to the Customer. The Company expenses incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that it would have recognized is one year or less.

Reserves for Variable Consideration

Revenue from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and which result from discounts, returns, chargebacks, rebates, co-pay assistance and other allowances that are offered within contracts between the Company and its Customers, health care providers, payors and other indirect customers relating to the Company's sales of its products. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amount will be credited to the Customer) or as a current liability (if the amount is payable to a Customer or a party other than a Customer). When appropriate, these estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as the Company's historical experience, current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which it is entitled based on the terms of the respective underlying contracts.

The amount of variable consideration that is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances: The Company generally provides Customers with discounts that include incentive fees that are explicitly stated in the Company's contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, the Company compensates (through trade discounts and allowances) its Customers for sales order management, data, and distribution services. However, the Company has determined such services received to date are not distinct from the Company's sale of products to the Customer and, therefore, these payments have been recorded as a reduction of revenue within the statement of operations and comprehensive loss through December 31, 2018. The Company records a corresponding reduction of accounts receivable (if the trade discount and/or allowance will be credited to the Customer) or an increase in accrued expense (if the trade discount and/or allowance is payable to a Customer) on the consolidated balance sheets.

Product Returns: Consistent with industry practice, the Company generally offers Customers a limited right of return which allows for the product to be returned when the product expiry is within an allowable window. This right of return lapses once the product is provided to a patient. The Company estimates the amount of its product sales that may be returned by its Customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized. The Company currently estimates product return reserve using available industry data and its own historical sales information, including its visibility into the inventory remaining in the distribution channel.

Provider Chargebacks and Discounts: Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to Customers who directly purchase the product from the Company. Customers charge the Company for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by Customers, and the Company generally issues credits for such amounts within a few weeks of the Customer's resale of the product. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel at each reporting period end that the Company expects will be sold to qualified healthcare providers, and chargebacks that Customers have claimed but for

which the Company has not yet issued a credit.

Commercial and Medicare Part D Rebates: The Company contracts with various commercial payor organizations, primarily health insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of its products. The Company estimates the rebates for commercial and Medicare Part D payors based upon (i) its contracts with the payors and (ii) information obtained from its Customers and other third parties regarding the payor mix for Auryxia. The Company estimates these rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Other Government Rebates: The Company is subject to discount obligations under state Medicaid programs and other government programs. The Company estimates its Medicaid and other government programs rebates based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the consolidated balance sheets. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability under the Medicare Part D program. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

Other Incentives: Other incentives that the Company offers include voluntary patient assistance programs such as the Company's co-pay assistance program, which are intended to provide financial assistance to qualified commercially insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on actual claims processed during a given period, as well as historical utilization data to estimate the amount the Company expects to receive associated with product that has been recognized as revenue, but remains in in the distribution channel at the end of each reporting period.

Collaboration Revenues

The Company enters into out-license and collaboration agreements which are within the scope of ASC 606, under which it licenses certain rights to its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, up-front license fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services the Company provides through its contract manufacturers; and royalties on net sales of licensed products. Each of these payments may result in license, collaboration and other revenue, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its agreements, the Company implements the five-step model noted above. As part of the accounting for these arrangements, the Company must develop assumptions that require judgment to determine whether the individual deliverables should be accounted for as separate performance obligations or as a combined performance obligation, and to determine the stand-alone selling price for each performance obligation identified in the contract. A deliverable represents a separate performance obligation if both of the following criteria are met: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer, and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract. The Company uses key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates, and probabilities of technical and regulatory success. With regard to the MTPC and Otsuka collaboration agreements, the Company recognizes revenue related to amounts allocated to the identified performance obligation on a proportional performance basis as the underlying services are performed.

Licenses of Intellectual Property

If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of

the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company will evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone Payments

At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to assess the milestone as probable of being achieved. There is considerable judgment involved in determining whether a milestone is probable of being reached at each specific reporting period. Milestone payments that are not within the control of the Company or the customer, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenues as, or when, the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company will re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue in the period of adjustment.

Manufacturing Supply Services

Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. The Company assesses if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations. If the Company is entitled to additional payments when the licensee exercises these options, any additional payments are recorded in license, collaboration and other revenues when the licensee obtains control of the goods, which is upon delivery.

Royalties

The Company will recognize sales-based royalties, including milestone payments based on the level of sales, at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). The Company receives royalty payments from JT and Torii, based on net sales of Riona in Japan.

Collaborative Arrangements

The Company records the elements of its collaboration agreements that represent joint operating activities in accordance with ASC Topic 808, Collaborative Arrangements (ASC 808). Accordingly, the elements of the collaboration agreements that represent activities in which both parties are active participants and to which both parties are exposed to the significant risks and rewards that are dependent on the commercial success of the activities are recorded as collaborative arrangements. The Company considers the guidance in ASC 606-10-15, Revenue from Contracts with Customers – Scope and Scope Exceptions, in determining the appropriate treatment for the transactions between the Company and its collaborative partner and the transactions between the Company and third parties. Generally, the classification of transactions under the collaborative arrangements is determined based on the nature and contractual terms of the arrangement along with the nature of the operations of the participants. Therefore, the Company recognizes its allocation of the shared costs incurred with respect to the jointly conducted medical affairs and commercialization and non-promotional activities under the U.S. collaboration with Otsuka as a component of the related expense in the period incurred. During the year ended December 31, 2018, the Company incurred approximately $1.2 million of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement, as defined below in Note 4, of which approximately $0.5 million are reimbursable by Otsuka and recorded as a reduction to research and development expense. During the year ended December 31, 2018, Otsuka incurred approximately $1.1 million of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement, of which approximately $0.5 million are reimbursable by the Company and recorded as an increase to research and development expense. To the extent product revenue is generated from the collaboration, the Company will recognize its share of the net sales on a gross basis if it is deemed to be the principal in the transactions with customers, or on a net basis if it is instead deemed to be the agent in the transactions with customers, consistent with the guidance in ASC 606.

Business Combinations

The Company accounts for the acquisition of a business in accordance with ASC Topic 805, Business Combinations, or ASC 805. Amounts paid for each acquisition are allocated to the assets acquired and liabilities assumed based on their fair values at the date of acquisition. The Company determines the fair value of acquired intangible assets based on detailed valuations that use certain information and assumptions provided by management, which is considered management's best estimate of inputs and assumptions that a market participant would use. The Company allocates any excess purchase price over the fair value of the net tangible and intangible assets acquired to goodwill.

Under ASC 805, transaction costs are not included as a component of consideration transferred and are expensed as incurred. Additionally, in accordance with ASC 805, a transaction entered into by or on behalf of the acquirer or primarily for the benefit of the acquirer or the combined entity, rather than primarily for the benefit of the acquiree (before the combination), is treated as separate transaction.

Intangible Assets

The Company maintains definite-lived intangible assets related to developed product rights for Auryxia and a favorable contract, which were acquired on December 12, 2018 as part of the Merger.

Intangible assets are initially recorded at fair value and stated net of accumulated amortization and impairments. The Company amortizes its intangible assets that have finite lives using either the straight-line method, or if reliably determinable, based on the pattern in which the economic benefit of the asset is expected to be utilized. Amortization for the Company’s intangible assets are recorded over their estimated useful live of 4 - 9 years.

The Company reviews intangible assets subject to amortization to determine if any adverse conditions exist or a change in circumstances has occurred that would indicate impairment or a change in the remaining useful life. If an impairment indicator exists, the Company performs a recoverability test by comparing the sum of the estimated undiscounted cash flows of the intangible asset to its carrying value on the consolidated balance sheet. If the carrying value of the intangible asset exceeds the undiscounted cash flows used in the recoverability test, the Company will write the carrying value down to the fair value in the period identified. The Company calculates the fair value of intangible assets as the present value of estimated future cash flows expected to be generated from the intangible asset using a risk-adjusted discount rate. In determining estimated future cash flows associated with its intangible assets, the Company uses market participant assumptions pursuant to ASC 820.

Goodwill

The Company allocates any excess purchase price over the fair value of the net tangible and intangible assets acquired in a business combination to goodwill. Goodwill is evaluated for impairment on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist.

The Company compares the fair value of its reporting unit to its carrying value. If the carrying value of the net assets assigned to the reporting unit exceeds the fair value of its reporting unit, the Company would record an impairment loss equal to the difference. As described above, the Company operates in one operating segment which the Company considers to be the only reporting unit.

Fair Value of Financial Instruments

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. ASC Topic 820, Fair Value Measurements and Disclosures, or ASC 820, establishes a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available.

Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments, and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described below:

- Level 1 – Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.
- Level 2 – Valuations based on quoted prices for similar assets or liabilities in markets that are not active, or for which all significant inputs are observable, either directly or indirectly.
- Level 3 – Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Items measured at fair value on a recurring basis include available for sale securities (see Note 7). The carrying amounts of prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair

values due to their short-term maturities. The rate implicit within the Company's capital lease obligation approximates market interest rates.

Items measured at fair value on a nonrecurring basis include property and equipment, intangible assets and goodwill. The Company remeasures the fair value of these assets upon the occurrence of certain events. There were no such remeasurements to property and equipment for the year ended December 31, 2018. There were no impairments to assets measured using level 3 inputs in fiscal year 2018 or 2017.

The Company's other financial instruments mainly consists of debt (see Note 11). The carrying amounts for the amount drawn on the Company's line of credit facility with Silicon Valley Bank approximates fair value because the interest rate is variable and reflects current market rates.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses are comprised of costs incurred in providing research and development activities, including salaries and benefits, facilities costs, overhead costs, contract research and development services, and other outside costs. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

External research and development expenses associated with the Company's programs include clinical trial site costs, research compounds and clinical manufacturing costs, costs incurred for consultants and other outside services, such as data management and statistical analysis support, and materials and supplies used in support of the clinical and preclinical programs. Internal costs of the Company's clinical program include salaries, benefits, stock-based compensation, and an allocation of the Company's facility costs. When third-party service providers' billing terms do not coincide with the Company's period-end, the Company is required to make estimates of its obligations to those third parties, including clinical trial and pharmaceutical development costs, contractual services costs and costs for supply of its drug candidates, incurred in a given accounting period and record accruals at the end of the period. The Company bases its estimates on its knowledge of the research and development programs, services performed for the period, past history for related activities and the expected duration of the third-party service contract, where applicable.

Advertising Expenses

The costs of advertising are expensed as incurred and included in selling, general and administrative expenses in the consolidated statements of operations and comprehensive loss. For the year ended December 31, 2018, advertising expenses totaled $0.5 million. The Company did not incur any advertising expenses for the years ended December 31, 2017 and 2016.

Income Taxes

Income taxes are recorded in accordance with FASB Topic 740, Income Taxes, or ASC 740, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided, if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. All deferred taxes as of December 31, 2018 and 2017 are classified as noncurrent within the income tax provision (see Note 14).

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position, as well as consideration of the available facts and circumstances. As of December 31, 2018 and 2017, the Company does not have any significant uncertain tax positions. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, Compensation—Stock Compensation, or ASC 718. ASC 718 requires all stock-based payments to employees, including

grants of employee stock options, restricted stock, restricted stock units, or RSUs, and modifications to existing stock awards, to be recognized in the statements of operations and comprehensive loss based on their fair values. The Company accounts for stock-based awards to non-employees in accordance with ASC Topic 505-50, Equity-Based Payments to Non-Employees, or ASC 505-50, which requires the fair value of the award to be re-measured at fair value until a performance commitment is reached or counterparty performance is complete. The Company's stock-based awards are comprised of stock options, shares of restricted stock, shares of common stock and warrants. The Company estimates the fair value of options granted using the Black-Scholes option pricing model. The Company uses a blend of its stock price and the quoted market price of comparable public companies to determine the fair value of restricted stock awards and common stock awards.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the lack of company-specific historical and implied volatility data for trading the Company's stock in the public market, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to the Company, including stage of product development and life science industry focus. During 2017, the Company began to estimate its volatility by using a blend of its stock price history for the length of time it has market data for its stock and the historical volatility of similar public companies for the expected term of each grant. The Company is a commercial-stage biopharmaceutical company and the representative group of companies has certain similar characteristics to the Company. The Company believes the group selected has sufficient similar economic and industry characteristics and includes companies that are most representative of the Company. The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock, which is similar to the Company's peer group.

The Company's stock-based awards are subject to either service- or performance-based vesting conditions. Compensation expense related to awards to employees with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term, and is adjusted for pre-vesting forfeitures in the period in which the forfeitures occur. Consistent with the guidance in ASC 505- 50, compensation expense related to awards to non-employees with service-based vesting conditions is recognized on a straight-line basis based on the then-current fair value at each financial reporting date prior to the measurement date over the associated service period of the award, which is generally the vesting term. Compensation expense related to awards to employees with performance-based vesting conditions is recognized based on the grant date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable. Consistent with the guidance in ASC 505-50, compensation expense related to awards to non-employees with performance-based vesting conditions is recognized based on the then-current fair value at each financial reporting date prior to the measurement date over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

For awards with performance conditions in which the award does not vest unless the performance condition is met, the Company recognizes expense if, and to the extent that, the Company estimates that achievement of the performance condition is probable. If the Company concludes that vesting is probable, it recognizes expense from the date it reaches this conclusion through the estimated vesting date.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted-average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted-average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the diluted net loss per share calculation, preferred stock,

stock options, warrants, restricted stock and RSUs are considered to be common stock equivalents, but have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented. Diluted net income per share is calculated by dividing the net income by the weighted-average common shares outstanding for the period, including any dilutive effect from outstanding options, warrants, restricted stock and RSUs using the treasury stock method.

3. Product Revenue, Net

The Company began recording product revenue from the U.S. sales of Auryxia on December 12, 2018 following the consummation of the Merger. Total net product revenue was $6.8 million for the period from December 12, 2018 to December 31, 2018. The following table summarizes activity in each of the product revenue allowance and reserve categories for the period from December 12, 2018 to December 31, 2018 (in thousands):

| | Chargebacks and Discounts | Rebates, Fees and other Deductions | Returns | Total |
|---|---|---|---|---|
| Balance at December 12, 2018 | $ 466 | $ 21,247 | $ 418 | $22,131 |
| Provisions related to sales | 415 | 3,869 | (58) | 4,226 |
| Credits/payments made relating to sales | (365) | (2,255) | — | (2,620) |
| Balance at December 31, 2018 | $ 516 | $ 22,861 | $ 360 | $23,737 |

Chargebacks, discounts and returns are recorded as a direct reduction of revenue on the consolidated statement of operations with a corresponding reduction to accounts receivable on the consolidated balance sheets. Rebates, distribution-related fees, and other sales-related deductions are recorded as a reduction in revenue on the consolidated statement of operations with a corresponding increase to accrued liabilities or accounts payable on the consolidated balance sheets.

4. License, Collaboration and Other Significant Agreements

The Company recognized $200.9 million, $181.2 million and $1.5 million in license, collaboration and other revenue for the years ended December 31, 2018, 2017 and 2016, respectively. The $200.9 million in license, collaboration and other revenue for the year ended December 31, 2018 included $200.5 million of the transaction price for the Company’s collaboration agreements with MTPC and Otsuka (discussed below), all of which are recognized based on a proportional performance method, approximately $0.3 million for other services related to clinical and regulatory related activities performed by the Company on behalf of MTPC that are not included in the performance obligations identified under the MTPC Agreement, and $0.1 million for license revenue related to royalties received from JT and Torii based on their sales of Riona in Japan. The $181.2 million in license, collaboration and other revenue for the year ended December 31, 2017 included $181.2 million of the transaction price for the MTPC Agreement and the Company’s collaboration agreements with Otsuka and approximately $31,000 for other services related to clinical and regulatory related activities performed by the Company on behalf of MTPC that are not included in the performance obligations identified under the MTPC Agreement. The $1.5 million in license and collaboration revenue for the year ended December 31, 2016 related to the transaction price for the Company’s collaboration agreement with Otsuka in the U.S.

During the years ended December 31, 2018, 2017 and 2016, the Company recognized the following revenues from its license, collaboration and other significant agreements and had the following deferred revenue balances as of December 31, 2018:

| | For the Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| License, Collaboration and Other Revenue: | (in thousands) | | |
| MTPC Agreement | $9,281 | $42,918 | $— |
| Otsuka U.S. Agreement | 103,870 | 85,971 | 1,535 |
| Otsuka International Agreement | 87,320 | 52,307 | — |
| Total Proportional Performance Revenue | $200,471 | $181,196 | $1,535 |
| JT and Torii | 112 | — | — |
| MTPC Stability Studies | 335 | 31 | — |
| Total License, Collaboration and Other Revenue | $200,918 | $181,227 | $1,535 |

| | December 31, 2018 | | |
|---|---|---|---|
| | Short-Term | Long-Term | Total |
| Deferred Revenue: | (in thousands) | | |
| Otsuka U.S. Agreement | $33,451 | $ 29,909 | $63,360 |
| Otsuka International Agreement | 23,529 | 21,121 | 44,650 |
| Vifor Agreement | — | 4,679 | 4,679 |
| Total | $56,980 | $ 55,709 | $112,689 |

The following table presents changes in the Company's contract assets and liabilities during the years ended December 31, 2018 and 2017 (in thousands):

| | Balance at Beginning of Period | Additions | Deductions | Balance at End of Period |
|---|---|---|---|---|
| Twelve Months Ended December 31, 2018 | | | | |
| Contract assets: | | | | |
| Other current assets | $— | $531 | $(531) | $— |
| Accounts receivable[1] | $34,186 | $146,267 | $(178,866) | $1,587 |
| Contract liabilities: | | | | |
| Deferred revenue | $179,624 | $133,537 | $(200,472) | $112,689 |
| Accounts payable | $— | $17,919 | $(4,427) | $13,492 |
| | | | | |
| Twelve Months Ended December 31, 2017 | | | | |
| Contract assets - Accounts receivable[1] | $33,823 | $43,324 | $(42,961) | $34,186 |
| Contract liabilities - Deferred revenue | $197,289 | $163,562 | $(181,227) | $179,624 |

[1] Excludes accounts receivable from other services related to clinical and regulatory activities performed by the Company on behalf of MTPC that are not included in the performance obligations identified under the MTPC Agreement. These receivables represented approximately $5,000 and $30,000 of accounts receivables in the accompanying consolidated balance sheets as of December 31, 2018 and 2017, respectively. Also excludes approximately $15.1 million in accounts receivable related to amounts due to the Company from product sales which are included in the accompanying consolidated balance sheet as of December 31, 2018.

During the years ended December 31, 2018 and 2017, the Company recognized the following revenues as a result of changes in the contract asset and contract liability balances in the respective periods (in thousands):

| | For the Year Ended December 31, | |
|---|---|---|
| Revenue Recognized in the Period from: | 2018 | 2017 |
| Amounts included in deferred revenue at the beginning of the period | $137,726 | $125,454 |
| Performance obligations satisfied in previous periods | $6,659 | $275 |

The Company did not recognize revenues as a result of changes in contract assets or contract liabilities during the year ended December 31, 2016.

Mitsubishi Tanabe Pharma Corporation Collaboration Agreement

Summary of Agreement

On December 11, 2015, the Company and MTPC entered into a collaboration agreement, or the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to vadadustat in Japan and certain other Asian countries, collectively, the MTPC Territory. In addition, the Company will supply vadadustat for both clinical and commercial use in the MTPC Territory, subject to MTPC's option to manufacture commercial drug product in the MTPC Territory.

The Company and MTPC agreed that, instead of including Japanese patients in the Company's global Phase 3 program for vadadustat, MTPC would be the sponsor of a Phase 3 program for vadadustat in Japan. Following consultation with the Japanese Pharmaceuticals and Medical Devices Agency, or the PMDA, MTPC initiated its Phase 3 development program for vadadustat in Japanese patients in Japan in the fourth quarter of 2017, and reported top-line data for the two Phase 3 pivotal trials and data from the two supportive Phase 3 studies in March 2019. MTPC is responsible for the costs of the Phase 3 program in Japan and other studies required there, and will make no funding payments for the global Phase 3 program.

In consideration for the exclusive license and other rights contained in the MTPC Agreement, MTPC is obligated to make payments totaling up to $265.0 million, comprised of a $20.0 million upfront payment, up to $50.0 million in specified development and regulatory milestones, up to $175.0 million in specified commercial milestones, and a $20.0 million advance payment for Phase 2 studies in Japanese patients completed by the Company and reimbursable by MTPC, as well as tiered double-digit royalty payments of up to 20% on sales of vadadustat in the MTPC Territory, subject to reduction upon launch of a generic product on a country-by-country basis.

The Company completed its Phase 2 study of vadadustat in non-dialysis dependent, or NDD, Japanese patients in Japan and reported top-line data in the third quarter of 2017. The Company also announced top-line data of its Phase 2 study of vadadustat in dialysis-dependent, or DD, Japanese patients in Japan in the first quarter of 2018. The costs of these Phase 2 studies are reimbursable by MTPC. MTPC was obligated to reimburse the Company for costs to complete the Phase 2 studies in excess of the $20.0 million advance payment. The Company incurred approximately $20.5 million in Phase 2 costs through June 30, 2018 and did not incur any additional costs subsequent to June 30, 2018 as the studies have been completed. As a result, MTPC reimbursed the Company an additional approximately $0.5 million related to the two Phase 2 studies which was collected in the fourth quarter of 2018.

MTPC has sole responsibility for the commercialization of vadadustat in the MTPC Territory as well as for Medical Affairs (as defined in the MTPC Agreement) in the MTPC Territory. Akebia is responsible for manufacturing and supplying vadadustat for clinical use in the MTPC Territory. Akebia will enter into a supply agreement with MTPC for the commercial supply of vadadustat prior to commercial launch.

The Company and MTPC have established a joint steering committee pursuant to the MTPC Agreement to oversee development and commercialization of vadadustat in the MTPC Territory, including approval of any development or commercialization plans. Unless earlier terminated, the MTPC Agreement will continue in effect on a country-by-country basis until the later of the following: expiration of the last-to-expire patent covering vadadustat in such country in the MTPC Territory; expiration of marketing or regulatory exclusivity in such country in the MTPC Territory; or ten years after the first commercial sale of vadadustat in such country in the MTPC Territory. MTPC may terminate the MTPC Agreement upon twelve months' notice at any time after the second anniversary of the effective date of the MTPC Agreement. Either party may terminate the MTPC Agreement upon the material breach of the other party that is not cured within a specified time period or upon the insolvency of the other party.

MTPC is required to make certain milestone payments to the Company aggregating up to approximately $225.0 million upon the achievement of specified development, regulatory and commercial events. More specifically, the Company received $10.0 million in development milestone payments and is eligible to receive up to $40.0 million in regulatory milestone payments and up to $175.0 million in commercial milestone payments associated with aggregate sales of all products. Additionally, if vadadustat is commercialized, the Company would be entitled to receive tiered royalty payments in the low double digits based on a percentage of net sales. Royalty payments are subject to certain reductions, including upon the introduction of competitive products in certain instances. Royalties are due on a country-by-country basis from the date of first commercial sale of a licensed product in a country until the last to occur of: (i) the expiration of the last to expire valid claim within the intellectual property covering the licensed product, (ii) the expiration of marketing or regulatory exclusivity in such country, or (iii) the tenth anniversary of the first commercial sale of such licensed product in such country. Due to the uncertainty of pharmaceutical development and the high historical failure rates associated with drug development, although the Company has received $10.0 million in development milestones, no additional milestone or royalty payments may ever be received from MTPC.

In September 2017, the Company provided MTPC with an option to access data from the Company's global Phase 3 vadadustat program for payments to the Company of up to $25.0 million, which is in addition to the milestone payments described above.

Revenue Recognition

The Company evaluated the elements of the MTPC Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, MTPC, is a customer. The Company's arrangement with MTPC contains the following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop and commercialize vadadustat (the License Deliverable) in the MTPC Territory, (ii) clinical supply of vadadustat (the Clinical Supply Deliverable), (iii) knowledge transfer, (iv) Phase 2 dosing study research

services (the Research Deliverable), and (v) rights to future know-how.

The Company has identified two performance obligations in connection with its material promises under the MTPC Agreement. Factors considered in making the assessment of which material promises will be accounted for as separate performance obligations included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the good or service is highly interdependent or highly interrelated to the other elements in the arrangement, and whether there are other vendors that can provide the items. Additionally, the MTPC Agreement does not include a general right of return. The two performance obligations identified in connection with the Company's obligations under the MTPC Agreement are as follows:

(i) License, Research and Clinical Supply Performance Obligation

The License Deliverable is not distinct from the Clinical Supply Deliverable. More specifically, the license delivered to MTPC does not provide the right to manufacture vadadustat. MTPC therefore, is prohibited from manufacturing any licensed product during clinical trials. Accordingly, MTPC must obtain the clinical trial products from the Company, which significantly limits the ability for MTPC to use the license for their intended use in a way that generates economic benefits.

The License Deliverable is not distinct from the knowledge transfer because MTPC cannot fully utilize the license for its intended purpose without the corresponding information regarding know-how, development data and regulatory materials possessed by the Company.

The License Deliverable is not distinct from the Research Deliverable because MTPC cannot fully utilize the license for its intended purpose without the performance of the Phase 2 dosing studies. The Phase 2 dosing studies needed to be performed prior to the PMDA approving any Phase 3 study to be performed in the MTPC Territory. Furthermore, MTPC cannot benefit from the Phase 2 dosing studies without the license and the undelivered Phase 3 clinical supply.

The License Deliverable is not distinct from the clinical supply, knowledge transfer or Phase 2 studies. As a result, the License Deliverable, clinical supply, knowledge transfer and Phase 2 studies do not qualify for separation and have been combined as a single performance obligation (the License, Research and Clinical Supply Performance Obligation).

(ii) Rights to Future Know-How Performance Obligation

The License, Research and Clinical Supply Deliverables combined are distinct from the rights to future know-how because MTPC can obtain the value of the License, Research and Clinical Supply Deliverables without receipt of any rights to future know-how that may be discovered or developed in the future. As a result, the rights to future know-how qualify for separation from the License, Research and Clinical Supply Performance Obligation.

The Company allocates the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of the standalone selling price for the Rights to Future Know-How Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement. The Company did not develop a best estimate of standalone selling price for the License, Research and Clinical Supply Performance Obligation because the estimate of standalone selling price associated with the Rights to Future Know-How Performance Obligation was determined to be immaterial. The Company has concluded that a change in the key assumptions used to determine the best estimate of standalone selling price for each performance obligation would not have a significant impact on the allocation of arrangement consideration.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the estimated cost for the Phase 2 studies, (iii) a non-substantive milestone associated with the first patient enrolled in the NDD-CKD Phase 3 study, and (iv) the cost of all clinical supply provided to MTPC for the Phase 3 studies. No other development and no regulatory milestones have been included in the transaction price at inception, as all other milestone amounts were fully

constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. The total aggregate amount of development milestones is $10.0 million and the total aggregate amount of the regulatory milestones is up to $40.0 million. The total aggregate amount of sales milestones is up to $175.0 million. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to MTPC and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

No amounts were allocated to the Rights to Future Know-How Performance Obligation because the associated best estimate of standalone selling price was determined to be immaterial; therefore the arrangement consideration will be allocated to the License, Research and Clinical Supply Performance Obligation.

As of December 31, 2018, the transaction price is comprised of: (i) the up-front payment of $20.0 million, (ii) the cost for the Phase 2 studies of $20.5 million, (iii) the cost of all clinical supply provided to MTPC for the Phase 3 studies, and (iv) $10.0 million in development milestones received, comprised of a $6.0 million and a $4.0 million development milestone. All development milestones have been reached as of December 31, 2018. No regulatory milestones have been assessed as probable of being reached as of December 31, 2018 and thus have been fully constrained. Revenue for the License, Research and Clinical Supply Performance Obligation for the MTPC Agreement is being recognized using a proportional performance method using the Company's delivery of clinical supply of vadadustat to MTPC for the Phase 3 study as the basis for recognition. The Company recognized $9.3 million in revenue during the year ended December 31, 2018, with respect to the MTPC Agreement, and approximately $42.9 million during the year ended December 31, 2017. The revenue is classified as collaboration revenue in the accompanying consolidated statements of operations. No revenue was recognized in 2016 with respect to the MTPC Agreement as the applicable revenue recognition criteria was not satisfied until 2017. As of December 31, 2018, there is no deferred revenue and no accounts receivable.

U.S. Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

Summary of Agreement

On December 18, 2016, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement. The collaboration is focused on the development and commercialization of vadadustat in the United States. Under the terms of the Otsuka U.S. Agreement, the Company is responsible for leading the development of vadadustat, including the ongoing Phase 3 development program. The Company and Otsuka will co-commercialize vadadustat in the United States, subject to the approval of vadadustat by the FDA.

Under the terms of the Otsuka U.S. Agreement, the Company granted to Otsuka a co-exclusive, non-sublicensable license under certain intellectual property controlled by the Company solely to perform medical affairs activities and to conduct non-promotional and commercialization activities related to vadadustat in accordance with the associated plans. The co-exclusive license relates to activities that will be jointly conducted by the Company and Otsuka pursuant to the terms of the Otsuka U.S. Agreement. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the agreement.

Pursuant to the terms of the Otsuka U.S. Agreement, the Company is responsible for performing all activities related to the development of vadadustat as outlined in the current global development plan. The current global development plan encompasses all activities with respect to the ongoing $PRO_2TECT$ and $INNO_2VATE$ clinical programs through the filing for marketing approval, as well as certain other studies. Under the Otsuka U.S. Agreement, subject to the terms of the Otsuka Funding Option, as described below, the Company controls and retains final decision making authority with respect to, among other things, the development of vadadustat. The Company's obligations related to the conduct of the current global development plan include the associated manufacturing and supply services for vadadustat.

Under the Otsuka U.S. Agreement, the parties jointly conduct, and have equal responsibility for, all medical affairs, commercialization and non-promotional activities pursuant to underlying plans as agreed to by the parties. If approved by the FDA, the Company will provide vadadustat to Otsuka for commercialization pursuant to a separate supply agreement to be negotiated.

The activities under the Otsuka U.S. Agreement are governed by a joint steering committee, or JSC, formed by an equal number of representatives from the Company and Otsuka. The JSC coordinates and monitors the parties' activities under the collaboration. Among other responsibilities, the JSC manages the overall strategic alignment between the parties, oversees the current global development plan and reviews other detailed plans setting forth the parties' activities under the arrangement, including the medical affairs plan and commercialization and non-promotional activities plan. Additionally, the parties established a joint development committee, or JDC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JDC shares information related to, and reviews and discusses activities and progress under, the current global development plan and any other development that may be conducted pursuant to the collaboration. The Company and Otsuka also established a joint manufacturing committee, or JMC, which is comprised of an equal number of representatives from each of the parties. Among other responsibilities, the JMC oversees the manufacturing plan and related manufacturing activities. In support of the potential commercialization of vadadustat, the parties established a joint commercialization committee, or JCC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JCC oversees the activities and progress under the commercialization and non-promotional activities plan and all other sales and marketing activities. Subject to the terms of the Otsuka Funding Option, as described below, the Company has retained final decision  making authority with respect to all development matters, U.S. pricing strategy and certain other key commercialization matters.

Under the terms of the Otsuka U.S. Agreement, the Company received a $125.0 million up-front, non-refundable, non-creditable cash payment in December 2016. In March 2017, the Company received a payment of approximately $33.8 million, which represents reimbursement for Otsuka's share of costs previously incurred by the Company in implementing the current global development plan through December 31, 2016. Commencing in the third quarter of 2017, whereupon the Company had incurred a specified amount of incremental costs, Otsuka began to contribute, as required by the Otsuka U.S. Agreement, a percentage of the remaining costs incurred under the current global development plan. The Company estimates that Otsuka's funding of the current global development plan costs subsequent to December 31, 2016 will total $167.5 million or more, depending on the actual costs incurred toward the current global development plan. The costs associated with the performance of any development activities in addition to those outlined in the current global development plan will be subject to a cost sharing or reimbursement mechanism to be determined by the parties. Costs incurred with respect to medical affairs and commercialization and non-promotional activities will generally be shared equally by the parties. In addition, if the costs incurred in completing the activities under the current global development plan exceed a certain threshold, or the Cost Threshold, then the Company may elect to require Otsuka to increase the aggregate percentage of current global development costs it funds under the Otsuka U.S. Agreement and the Otsuka International Agreement, as defined below, from 52.5% to 80%, or the Otsuka Funding Option. In such event, the excess of the payments made under such election and Otsuka's allocated share of the current global development costs is fully creditable against future payments due to the Company under the arrangement, provided that future payments due to the Company may not be reduced by more than 50% in any calendar year and any remaining creditable amount above 50% in any calendar year will be applied to subsequent future payments until fully credited. In addition, decisions regarding certain development matters will be made jointly by the Company and Otsuka in accordance with the procedures set forth in the Otsuka U.S. Agreement. In September 2018, the Company exercised the Otsuka Funding Option, which will be effective when the Cost Threshold is exceeded. The Company estimates that the Cost Threshold will be exceeded in the second quarter of 2019.

In addition, Otsuka would be required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial events. More specifically, the Company is eligible to receive up to $125.0 million in development milestone payments and up to $65.0 million in regulatory milestone payments for the first product to achieve the associated event. Moreover, the Company is eligible for up to $575.0 million in commercial milestone payments associated with aggregate sales of licensed products, subject to reduction as set forth above. Due to the uncertainty of pharmaceutical development and the high historical failure rates associated therewith, no milestone payments may ever be received from Otsuka.

Under the Otsuka U.S. Agreement, the Company and Otsuka share the costs of developing and commercializing vadadustat in the United States and the profits from the sales of vadadustat after approval by the FDA. In connection with the profit share calculation, net sales include gross sales to third-party customers net of discounts, rebates, chargebacks, taxes, freight and insurance charges and other applicable deductions. Shared costs generally include costs attributable or reasonably allocable to the manufacture of vadadustat for commercialization purposes and the performance of medical affairs activities, non-promotional activities and commercialization activities.

Unless earlier terminated, the Otsuka U.S. Agreement will expire in the U.S. on a product-by-product basis on the date that one or more generic versions of vadadustat first achieves 90% market penetration. Either party may terminate the Otsuka U.S. Agreement in its entirety upon an uncured breach or insolvency on the part of the other party. Otsuka may terminate the Otsuka U.S. Agreement in its entirety upon 12 months' prior written notice at any time after the release of the first topline data from the global Phase 3 development program for vadadustat. In the event of termination of the Otsuka U.S. Agreement, all rights and licensees granted to Otsuka under the Otsuka U.S. Agreement will automatically terminate and the licenses granted to the Company will become freely sublicensable. In addition, the upfront payment, all development costs and milestone payments received by the Company prior to such termination will not be refunded to Otsuka.

Revenue Recognition

The Company evaluated the elements of the Otsuka U.S. Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, Otsuka, is a customer. The Company's arrangement with Otsuka contains the following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop, perform medical affairs activities with respect to and conduct non-promotional and commercialization activities related to vadadustat and products containing or comprising vadadustat (the License Deliverable), (ii) development services to be performed pursuant to the current global development plan (the Development Services Deliverable), (iii) rights to future intellectual property (the Future IP Deliverable), and (iv) joint committee services (the Committee Deliverable).

The Company has identified three performance obligations in connection with its obligations under the Otsuka U.S. Agreement. Factors considered in making the assessment of which material promises will be accounted for as separate performance obligations included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the good or service is highly interdependent or highly interrelated to the other elements in the arrangement, and whether there are other vendors that can provide the items. Additionally, the Otsuka U.S. Agreement does not include a general right of return. The three performance obligations identified in connection with the Company's obligations under the Otsuka U.S. Agreement are as follows:

(i) License and Development Services Combined (License Performance Obligation)
The License Deliverable is not distinct from the Development Services Deliverable, due to the limitations inherent in the license conveyed. More specifically, the license conveyed to Otsuka does not provide Otsuka with the right to manufacture vadadustat and products containing or comprising vadadustat. However, the manufacturing and supply services that are conducted as part of the services to be performed pursuant to the current global development plan are necessary for Otsuka to fully exploit the associated license for its intended purpose. The value of the rights provided through the license conveyed will be realized when the underlying products covered by the intellectual property progress through the development cycle, receive regulatory approval and are commercialized. Products containing or comprising vadadustat cannot be commercialized until the development services under the current global development plan are completed. Accordingly, Otsuka must obtain the manufacturing and supply of the associated products that are included within the development services to be performed pursuant to the current global development plan from the Company in order to derive benefit from the license, which significantly limits the ability for Otsuka to utilize the License Deliverable for its intended purpose in a way that generates economic benefits.

(ii) Rights to Future Intellectual Property (Future IP Performance Obligation)
The License and Development Services deliverables combined are distinct from the Future IP Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development services without the receipt of any other intellectual property that may be discovered or developed in the future. The Future IP Deliverable is distinct from the Committee Deliverable because the joint committee services have no bearing on the value to be derived from the rights to potential future intellectual property. As a result, the Future IP Deliverable qualifies as a separate performance obligation.

(iii) Joint Committee Services (Committee Performance Obligation)
The License and Development Services deliverables combined are distinct from the Committee Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development services without the joint committee services. The Committee Deliverable also is distinct from the rights to Future IP Deliverable because the joint committee services have no bearing on the value to be derived from the rights to potential future intellectual property. As a result, the Committee Deliverable qualifies as a separate performance obligation.

The Company allocates the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of standalone selling price for the Committee Performance Obligation after considering the nature of the services to be performed and estimates of the associated effort and rates applicable to such services that would be expected to be realized under similar contracts. The Company developed a best estimate of standalone selling price for the Future IP Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement. The Company did not develop a best estimate of standalone selling price for the License Performance Obligation due to the following: (i) the best estimates of standalone selling price associated with the Future IP Performance Obligation was determined to be immaterial and (ii) the period of performance and pattern of recognition for the License Performance Obligation and the Committee Performance Obligation was determined to be similar. The Company has concluded that a change in the key assumptions used to

determine the best estimate of standalone selling price for each performance obligation would not have a significant impact on the allocation of arrangement consideration.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the cost share payment with respect to amounts incurred by the Company through December 31, 2016, and (iii) an estimate of the cost share payments to be received with respect to amounts incurred by the Company subsequent to December 31, 2016. No development or regulatory milestones were included in the transaction price at inception, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Otsuka and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

No amounts were allocated to the Future IP Performance Obligation because the associated best estimate of standalone selling price was determined to be immaterial. Due to the similar performance period and recognition pattern between the License Performance Obligation and the Committee Performance Obligation, the transaction price has been allocated to the License Performance Obligation and the Committee Performance Obligation on a combined basis. Accordingly, the Company will recognize revenue related to the allocable arrangement consideration on a proportional performance basis as the underlying development services are performed pursuant to the current global development plan which is commensurate with the period and consistent with the pattern over which the Company's obligations are satisfied for both the License Performance Obligation and the Committee Performance Obligation. Effectively, the Company has treated the arrangement as if the License Performance Obligation and the Committee Performance Obligation are a single performance obligation.

As of December 31, 2018, the transaction price totaling $326.3 million is comprised of: (i) the up-front payment of $125.0 million, (ii) the cost share payment with respect to amounts incurred by the Company through December 31, 2016 of $33.8 million, and (iii) the estimate of the cost share payments to be received of approximately $167.5 million with respect to amounts incurred by the Company subsequent to December 31, 2016. As of December 31, 2018, no development or regulatory milestones have been assessed as probable of being reached and thus have been fully constrained.

During the years ended December 31, 2018, 2017 and 2016, the Company recognized revenue totaling approximately $103.9 million, $86.0 million and $1.5 million, respectively, with respect to the Otsuka U.S. Agreement. The revenue is classified as collaboration revenue in the accompanying consolidated statements of operations. As of December 31, 2018, there is approximately $63.4 million of deferred revenue related to the Otsuka U.S. Agreement of which $33.5 million is classified as current and $29.9 million is classified as long-term in the accompanying consolidated balance sheet based on the performance period of the underlying obligations. Additionally, as of December 31, 2018, there is approximately $7.2 million in contract liabilities (included in accounts payable) in the accompanying consolidated balance sheet.

The Company determined that the medical affairs, commercialization and non-promotional activities elements of the Otsuka U.S. Agreement represent joint operating activities in which both parties are active participants and of which both parties are exposed to significant risks and rewards that are dependent on the success of the activities. Accordingly, the Company is accounting for the joint medical affairs, commercialization and non-promotional activities in accordance with ASC No. 808, Collaborative Arrangements (ASC 808). Additionally, the Company has determined that in the context of the medical affairs, commercialization and non-promotional activities, Otsuka does not represent a customer as contemplated by ASC 606-10-15, Revenue from Contracts with Customers – Scope and Scope Exceptions. As a result, the activities conducted pursuant to the medical affairs, commercialization and non-promotional activities plans will be accounted for as a component of the related expense in the period incurred. During the year ended December 31, 2018, the Company incurred approximately $1.2 million of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement of which approximately $0.5 million are reimbursable by Otsuka and recorded as a reduction to research and development expense during the year ended December 31, 2018. During the year ended December 31, 2018, Otsuka incurred approximately $1.1 million of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement, of which approximately $0.5 million are reimbursable by the Company and recorded as an increase to research and development expense during the year ended December 31, 2018.

International Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

Summary of Agreement

On April 25, 2017, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka International Agreement. The collaboration is focused on the development and commercialization of vadadustat in Europe, Russia, China, Canada, Australia, the Middle East and certain other territories, collectively, the Otsuka International Territory. Under the terms of the Otsuka International Agreement, the Company is responsible for leading the development of vadadustat, including the ongoing global Phase 3 development program. Otsuka has the sole responsibility, at its own cost, for the commercialization of vadadustat in the Otsuka International Territory, subject to the approval by the relevant regulatory authorities.

Under the terms of the Otsuka International Agreement, the Company granted to Otsuka an exclusive, sublicensable license under certain intellectual property controlled by the Company to develop and commercialize vadadustat and products containing or comprising vadadustat in the Otsuka International Territory.

Pursuant to the terms of the Otsuka International Agreement, the Company is responsible for performing all activities related to the development of vadadustat as outlined in the current global development plan; however, the parties may agree to allocate certain responsibilities to Otsuka. Under the Otsuka International Agreement, and subject to the terms of the Otsuka Funding Option described above, the Company controls and retains final decision-making authority with respect to, among other things, the development of vadadustat other than with respect to certain development matters specific to the Otsuka International Territory. Per the terms of the Otsuka International Agreement, Otsuka is generally responsible for the conduct of any development activities that may be required for marketing approvals in the Otsuka International Territory or otherwise performed with respect to the Otsuka International Territory that are incremental to those included in the current global development plan. The Company’s obligations related to the conduct of the current global development plan include the associated manufacturing and supply services for vadadustat.

Under the Otsuka International Agreement, Otsuka is to be solely responsible for the conduct of all medical affairs and commercialization activities in the Otsuka International Territory pursuant to underlying plans as reviewed and discussed by the parties. If approved by the relevant jurisdictional regulatory health authorities in the Otsuka International Territory, the Company will provide vadadustat to Otsuka for commercialization pursuant to a separate supply agreement to be negotiated. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the agreement.

The activities under the Otsuka International Agreement are governed by a JSC formed by an equal number of representatives from the Company and Otsuka. The JSC coordinates and monitors the parties' activities under the collaboration. Among other responsibilities, the JSC manages the overall strategic alignment between the parties, oversees the current global development plan and reviews other detailed plans setting forth any other development activities that may be conducted under the arrangement. Additionally, the parties established a JDC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JDC shares information related to, and reviews and discusses activities and progress under, the current global development plan and any other development that may be conducted pursuant to the collaboration. The Company and Otsuka also established a JMC, which is comprised of an equal number of representatives from each of the parties. Among other responsibilities, the JMC oversees the manufacturing plan and related manufacturing activities. In support of the potential commercialization of vadadustat, the parties established a JCC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JCC manages the activities and progress under the commercialization and non-promotional activities plan and all other sales and marketing activities. Subject to the terms of the Otsuka Funding Option described above, the Company has retained final decision making authority with respect to all development matters, other than decisions related to certain development matters specific to the Otsuka International Territory. Otsuka has retained final decision making authority with respect to all commercialization matters, other than decisions related to certain marketing matters.

Under the terms of the Otsuka International Agreement, the Company received a $73.0 million up-front, non-refundable, non-creditable cash payment. The Company also received a payment of approximately $0.2 million which represents reimbursement for Otsuka's share of costs previously incurred by the Company in implementing the current global development plan in excess of a specified threshold during the quarter ended March 31, 2017. Commencing in the second quarter of 2017, Otsuka began to contribute, as required by the Otsuka International Agreement, a percentage of the remaining costs incurred under the current global development plan. The Company estimates that Otsuka's funding of the current global development plan costs subsequent to March 31, 2017 will total roughly $176.1 million or more, depending on the actual current global development plan costs incurred. The costs associated with the performance of any mutually agreed upon development activities in addition to those outlined in the current global development plan will be subject to a cost sharing or reimbursement mechanism to be determined by the parties. Otsuka may elect to conduct additional studies of vadadustat in the EU, subject to the Company's right to delay such studies based on its objectives outside the Otsuka International Territory. Otsuka will pay a percentage of the costs of any such studies, and the Company will pay its portion of the costs in the form of a credit against future amounts due to the Company under the Otsuka International Agreement. The costs incurred related to any other development activities, which are pursued solely for obtaining or maintaining marketing approval in the Otsuka International Territory or otherwise performed solely with respect to the Otsuka International Territory that are incremental to the development activities included in the current global development plan, will be borne in their entirety by Otsuka. Otsuka will pay costs incurred with respect to medical affairs and commercialization activities in the Otsuka International Territory.

In addition, Otsuka would be required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial events. More specifically, the Company is eligible to receive up to $80.0 million in development milestone payments and up to $52.0 million in regulatory milestone payments for the first licensed product to achieve the associated event. Moreover, the Company is eligible for up to $525.0 million in

commercial milestone payments associated with aggregate sales of all licensed products. Additionally, to the extent vadadustat is commercialized, the Company would be entitled to receive tiered royalty payments ranging from the low double digits to the low thirties based on a percentage of net sales. Royalties are due on a country-by-country basis from the date of the first commercial sale of a licensed product in a country until the latest to occur of: (i) the expiration date in such country of the last to expire valid claim within the intellectual property covering the licensed product, (ii) the date of expiration of data or regulatory exclusivity in such country or (iii) the tenth anniversary of the first commercial sale of such licensed product in such country. Due to the uncertainty of pharmaceutical development and the high historical failure rates associated therewith, no milestone or royalty payments may ever be received from Otsuka. There are no cancellation, termination or refund provisions in the Otsuka International Agreement that contain material financial consequences to the Company.

Unless earlier terminated, the Otsuka International Agreement will expire upon the expiration of the royalty term in the last country in the Otsuka International Territory. Either party may terminate the Otsuka International Agreement in its entirety upon an uncured material breach or insolvency on the part of the other party. Otsuka may terminate the Otsuka International Agreement in its entirety or for a specific region in the Otsuka International Territory upon 12 months' prior written notice at any time after the release of the first topline data from either the PRO$_2$TECT Phase 3 development program or the INNO$_2$VATE Phase 3 development program, whichever comes first. In the event of termination of the Otsuka International Agreement, all rights and licensees granted to Otsuka under the Otsuka International Agreement will automatically terminate, and the licenses granted to the Company will become freely sublicensable, but potentially subject to a future royalty. In addition, the upfront payment, all development costs and milestone payments received by the Company prior to such termination will not be eligible for refund to Otsuka.

Revenue Recognition

The Company has accounted for the Otsuka International Agreement separately from the collaboration arrangement with Otsuka with respect to the U.S. due to the lack of interrelationship and interdependence of the elements and payment terms within each of the contracts as they relate to the respective territories. Accordingly, the Company has applied the guidance in ASC 606 solely in reference to the terms and conditions of the Otsuka International Agreement, while the Otsuka U.S. Agreement has continued to be accounted for as a discrete agreement in its own right. The Company evaluated the Otsuka International Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, Otsuka, is a customer. The Company's arrangement with Otsuka related to the Otsuka International Territory contains the following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop and commercialize (including the associated packaging) vadadustat and products containing or comprising vadadustat and development services to be performed pursuant to the current global development plan (the License and Development Services Deliverable), (ii) rights to future intellectual property (the Future IP Deliverable) and (iii) joint committee services (the Committee Deliverable).

The Company has identified three performance obligations in connection with its obligations under the Otsuka International Agreement. Factors considered in making this assessment of which material promises will be accounted for as a separate performance obligation included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the good or service is highly interdependent or highly interrelated to the other elements in the arrangement, and whether there are other vendors that can provide the items. Additionally, the Otsuka International Agreement does not include a general right of return. The three performance obligations identified in connection with the Company's obligations under the Otsuka International Agreement are as follows:

(i) License and Development Services Combined (License Performance Obligation)
The Company has determined that the license granted to Otsuka pursuant to the Otsuka International Agreement will be accounted for as component of the development services as opposed to a separately identified promise. Although the rights granted under the license are effective throughout the entire term of the arrangement, the Company will not be providing significant additional contributions of study data, regulatory submissions and regulatory approvals beyond the point that services under the current global development plan are conducted. Therefore, the period and pattern of recognition would be the same for both the license and the development services. Consequently, the Company has concluded that the license will effectively be treated as an inherent part of the associated development services promise instead of as a separate promise. As a result, the License and Development Services Deliverable will be treated as a single performance obligation (the License Performance Obligation).

(ii) Rights to Future Intellectual Property (Future IP Performance Obligation)
The License and Development Services Deliverable is distinct from the Future IP Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development services without the receipt of any other intellectual property that may be discovered or developed in the future. The Future IP Deliverable is distinct from the Committee Deliverable because the Committee Deliverable has no bearing on the value to be derived from the rights to potential future intellectual property. As a result, the Future IP Deliverable qualifies as a separate performance obligation.

(iii) Joint Committee Services (Committee Performance Obligation)
The License and Development Services Deliverable is distinct from the Committee Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development service without the joint committee services. The Committee Deliverable is distinct from the Future IP Deliverable because the Committee Deliverable has no bearing on the value to be derived from the rights to potential future intellectual property. As a result, the Committee Deliverable qualifies as a separate performance obligation.

The Company allocates the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of standalone selling price for the Committee Performance Obligation after considering the nature of the services to be performed and estimates of the associated effort and rates applicable to such services that would be expected to be realized under similar contracts. The Company developed a best estimate of standalone selling price for the Future IP Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement. The Company did not develop a best estimate of standalone selling price for the License Performance Obligation due to the following: (i) the best estimates of standalone selling price associated with the Future IP Performance Obligation was determined to be immaterial and (ii) the period of performance and pattern of recognition for the License Performance Obligation and the Committee Performance Obligation was determined to be similar. The Company has concluded that a change in the key assumptions used to determine the best estimate of standalone selling price for each performance obligation would not have a significant impact on the allocation of arrangement consideration.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the cost share payment with respect to amounts incurred by the Company during the quarter ended March 31, 2017, and (iii) an estimate of the cost share payments to be received with respect to amounts incurred by the Company subsequent to March 31, 2017. No development or regulatory milestones were included in the transaction price at inception, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including whether the receipt of the milestone payment is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Otsuka and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

No amounts were allocated to the Future IP Performance Obligation because the associated best estimate of standalone selling price was determined to be immaterial. Due to the similar performance period and recognition pattern between the License Performance Obligation and the Committee Performance Obligation, the transaction price has been allocated to the License Performance Obligation and the Committee Performance Obligation on a combined basis. Accordingly, the Company will recognize revenue related to the allocable arrangement consideration on a proportional performance basis as the underlying development services are performed pursuant to the current global development plan which is commensurate with the period and consistent with the pattern over which the Company's obligations are satisfied for both the License Performance Obligation and the Committee Performance Obligation. Effectively, the Company has treated the arrangement as if the License Performance Obligation and the Committee Performance Obligation are a single performance obligation.

As of December 31, 2018, the transaction price totaling $249.3 million is comprised of: (i) the up-front payment of $73.0 million, (ii) the cost share payment with respect to amounts incurred by the Company during the quarter ended March 31, 2017 of $0.2 million, and (iii) an estimate of the cost share payments to be received with respect to amounts incurred by the Company subsequent to March 31, 2017 of $176.1 million. As of December 31, 2018, no development or regulatory milestones have been assessed as probable of being reached and thus have been fully constrained.

During the years ended December 31, 2018 and 2017, the Company recognized revenue totaling approximately $87.3 million and $52.3 million, respectively, with respect to the Otsuka International Agreement. The revenue is classified as collaboration revenue in the accompanying consolidated statements of operations. As of December 31, 2018, there is approximately $44.6 million of deferred revenue related to the Otsuka International Agreement of which $23.5 million is classified as current and $21.1 million is classified as long-term in the accompanying consolidated balance sheet based on the performance period of the underlying obligations. Additionally, as of December 31, 2018, there is approximately $6.3 million in contract liabilities (included in accounts payable) in the accompanying consolidated balance sheet.

Janssen Pharmaceutica NV Research and License Agreement

Summary of Agreement

On February 9, 2017, the Company entered into a Research and License Agreement, the Janssen Agreement, with Janssen Pharmaceutica NV, or Janssen, a subsidiary of Johnson & Johnson, pursuant to which Janssen granted the Company an exclusive license under certain intellectual property rights to develop and commercialize worldwide certain HIF prolyl hydroxylase targeted compounds.

Under the terms of the Janssen Agreement, Janssen granted to the Company a license for a three-year research term to conduct research on the HIF compound portfolio, unless the Company elects to extend such research term for up to two additional one-year periods upon payment of an extension fee. During the research term, the Company may designate one or more compounds as candidates for development and commercialization. Once a compound is designated for development and commercialization, the Company will be solely responsible for the development and commercialization of the compound worldwide at its own cost and expense.

Under the terms of the Janssen Agreement, the Company made an upfront payment of $1.0 million in cash to Janssen and issued a warrant to purchase 509,611 shares of the Company's common stock. In addition, Janssen could be eligible to receive up to an aggregate of $16.5 million from the Company in specified development milestone payments on a product-by-product basis. Janssen will also be eligible to receive up to $215.0 million from the Company in specified commercial milestones as well as tiered, escalating royalties ranging from a low to mid-single digit percentage of net sales, on a product-by-product basis, and subject to reduction upon expiration of patent rights or the launch of a generic product in the territory.

Unless earlier terminated, the Janssen Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the last royalty term, which ends upon the longer of the expiration of the patents licensed under the Janssen Agreement, the expiration of regulatory exclusivity for such product, or 10 years from first commercial sale of such product. The Company may terminate the Janssen Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Janssen. The parties also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Janssen Agreement or in the event of certain additional circumstances.

As discussed above, the Company issued a Common Stock Purchase Warrant, or the Warrant, to Johnson & Johnson Innovation – JJDC, Inc., or JJDC, an affiliate of Janssen, for 509,611 shares of the Company's common stock at an exercise price of $9.81 per share. The Warrant is exercisable by JJDC, in whole or in part, at any time prior to February 9, 2022. The Warrant and the shares issuable upon exercise of the Warrant will be sold and issued without registration under the Securities Act of 1933, as amended, or the Securities Act. The Company recorded the fair value of the Warrant in the amount of $3.4 million to additional paid-in capital and research and development expense in March 2017.

Vifor Pharma License Agreement

Summary of Agreement

On May 12, 2017, the Company entered into a License Agreement, or the Vifor Agreement, with Vifor (International) Ltd., or Vifor Pharma, pursuant to which the Company granted Vifor Pharma an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, an affiliate of Fresenius Medical Care North America, in the United States.

The license grant under the Vifor Agreement is conditioned upon the approval of vadadustat for DD-CKD patients by the FDA, inclusion of vadadustat in a bundled reimbursement model, and payment by Vifor Pharma of a $20.0 million milestone upon the occurrence of these two events. The Vifor Agreement is structured as a profit share arrangement between the Company and Vifor Pharma in which the Company will receive a majority of the profit from Vifor Pharma's sales of vadadustat to FKC in the United States. The Company will share the milestone payment and the revenue from the profit share with Otsuka pursuant to the Otsuka U.S. Agreement. The Company retains all rights to commercialize vadadustat for use in the NDD-CKD market and in other dialysis organizations in the United States, which will be done in collaboration with Otsuka following FDA approval.

Prior to FDA approval of vadadustat, the Company and Vifor Pharma will enter into a commercial supply agreement for vadadustat pursuant to which the Company will supply all of Vifor Pharma's requirements for vadadustat in the United States. In addition, pursuant to the Vifor Agreement, Vifor Pharma entered into supply agreements that govern the terms pursuant to which Vifor Pharma would supply vadadustat to FKC for use in patients at its dialysis centers, subject to FDA approval; however, FKC is not obligated to utilize vadadustat in its clinics. During the term of the Vifor Agreement, Vifor Pharma will not sell to FKC or its affiliates any HIF product that competes with vadadustat in the United States.

Unless earlier terminated, the Vifor Agreement will expire upon the later of the expiration of all patents that claim or cover vadadustat, or expiration of data or regulatory exclusivity for vadadustat in the United States. Vifor Pharma may terminate the Vifor Agreement in its entirety upon 12 months' prior written notice after the release of the first topline data in the vadadustat global Phase 3 program for dialysis-dependent CKD patients. Either party may terminate the Vifor Agreement in the event of the other party's uncured material breach. The Company may also terminate the Vifor Agreement upon the occurrence of other events, such as for specific violations of the Vifor Agreement or if there are changes in Vifor Pharma's relationship with FKC.

Investment Agreement

In connection with the Vifor Agreement, in May 2017, the Company and Vifor Pharma entered into an investment agreement, or the Investment Agreement, pursuant to which the Company sold an aggregate of 3,571,429 shares of the Company's common stock, or the Shares, to Vifor Pharma at a price per share of $14.00 for a total of $50.0 million. The amount representing the premium over the closing stock price of $12.69 on the date of the transaction, totaling $4.7 million, was determined by the Company to represent consideration related to the Vifor Agreement. As the parties' rights under the Vifor Agreement are conditioned upon (a) the approval of vadadustat for DD-CKD patients by the FDA; (b) inclusion of vadadustat in a bundled reimbursement model; and (c) payment by Vifor Pharma of a $20.0 million milestone upon the occurrence of these two events, in accordance with ASC 606, the Company has determined that the full transaction price is fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including clinical and regulatory risks that must be overcome in order for the parties' rights to become effective and the probability of the $20.0 million milestone being achieved. Accordingly, the $4.7 million continues to be recorded as deferred revenue in the accompanying unaudited condensed consolidated balance sheets. Upon the satisfaction of the aforementioned conditions, revenue will be recognized as the Company supplies vadadustat to Vifor Pharma using a proportional performance method.

Vifor Pharma has agreed to a lock-up restriction such that it agrees not to sell the Shares for a period of time following the effective date of the Investment Agreement as well as a customary standstill agreement. In addition, the Investment Agreement contains voting agreements made by Vifor Pharma with respect to the Shares. The Shares have not been registered pursuant to the Securities Act, and were issued and sold in reliance upon the exemption from registration contained in Section 4(a)(2) of the Securities Act and Rule 506 promulgated thereunder.

License Agreement with Panion & BF Biotech, Inc

In connection with the Merger, the Company now has a license agreement with Panion & BF Biotech, Inc., or Panion, under which Keryx, our wholly owned subsidiary, remains the contracting party. Under the license agreement with Panion and the subsequent Amended and Restated License Agreement, collectively the Panion License Agreement, the Company in-licensed the exclusive worldwide rights, excluding certain Asian-Pacific countries, for the development and commercialization of ferric citrate. In addition, Panion is eligible to receive royalty payments based on a mid-single digit percentage of net sales of ferric citrate in the licensed territory.

The Panion License Agreement terminates upon the expiration of the Company's obligations to pay royalties thereunder. In addition, the Company may terminate the Panion License Agreement (i) in its entirety or (ii) with respect to one or more countries in the territory covered by the agreement, in either, case upon 90 days' notice. The Company and Panion also have the right to terminate the Panion License Agreement upon the occurrence of an uncured breach of a material provision of the Panion License Agreement and certain insolvency events.

On October 24, 2018, prior to the consummation of the Merger, Akebia and Keryx entered into a letter agreement with Panion, the Panion Letter Agreement, pursuant to which Panion agreed to rescind any and all prior termination threats or notices relating to the license agreement and waived its rights to terminate the license agreement based on any breach by Keryx of its obligation to use commercially reasonable efforts to commercialize Auryxia outside the United States until the parties execute an amendment to the license agreement in accordance with the terms of the Panion Letter Agreement following consummation of the Merger. These terms include establishing a joint steering committee consisting of Panion and Akebia representatives to oversee the development and commercialization of Fexeric in Europe and providing Panion with an exclusive license under Keryx-owned patents covering the rights to make, use, sell, offer for sale and import ferric citrate in certain countries in the Asia-Pacific region. The parties intend to work together to agree on a regulatory plan for Fexeric in Europe within four months after execution of the Panion Letter Agreement. The parties also intent to work together to agree on a commercialization plan for Fexeric in Europe following execution of the amendment. The amendment is expected to include alternatives in the event a commercialization plan is not agreed upon, such as payment of an annual license maintenance fee to Panion or the return of European intellectual property rights to Panion. Under the terms of the Panion Letter Agreement, Panion also agreed that Keryx will have the right, but not the obligation, to conduct any litigation against any infringer of patent rights under the license agreement on the terms agreed upon in the Panion Letter Agreement. In addition, Keryx made a $500,000 payment to Panion promptly after execution of the Panion Letter Agreement.

During the period from December 12, 2018 to December 31, 2018, the Company has incurred approximately $0.4 million in royalty payments due to Panion relating to Akebia sales of Auryxia in the United States and JT and Torii net sales of Riona in Japan, as the company is required to pay a low double-digit percent of sublicense income to Panion under the terms of the license agreement.

Sublicense Agreement with Japan Tobacco, Inc. and its subsidiary, Torii Pharmaceutical Co., Ltd.

Summary of Agreement

In connection with the Merger, the Company now has a Sublicense Agreement with JT and Torii, and the Amended and Restated Sublicense Agreement with JT and Torii, collectively the JT and Torii Sublicense Agreement, under which Keryx, our wholly owned subsidiary, remains the contracting party. Under the JT and Torii Sublicense Agreement, JT and Torii obtained the exclusive sublicense rights for the development and commercialization of ferric citrate in Japan. JT and Torii are responsible for the future development and commercialization costs in Japan.

Ferric citrate is currently approved by the Japanese Ministry of Health, Labour and Welfare for manufacturing and marketing in Japan for the treatment of hyperphosphatemia in patients with CKD. Ferric citrate is being marketed in Japan by Torii, under the brand name Riona. The Company is eligible to receive royalty payments based on a tiered double-digit percentage of net sales of Riona in Japan escalating up to the mid-teens, subject to certain reductions upon expiration or termination of the Amended and Restated License Agreement between Keryx and Panion & BF Biotech, Inc., or Panion, by which Keryx in-licensed the exclusive worldwide rights, excluding certain Asian-Pacific countries, for the development and commercialization of ferric citrate. The company is and is entitled to receive up to an additional $55.0 million upon the achievement of certain annual net sales milestones.

The sublicense terminates upon the expiration of all underlying patent rights. Also, JT and Torii may terminate the sublicense agreement with or without cause upon at least six months prior written notice to us. Additionally, either party may terminate the sublicense agreement for cause upon 60 days' prior written notice after the breach of any uncured material provision of the sublicense agreement, or after certain insolvency events.

Revenue Recognition

The Company evaluated the elements of the JT and Torii Sublicense Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, JT and Torii, is a customer. The Company's arrangement with JT and Torii contains the following material promises under the contract at inception: (i) exclusive license to develop and commercialize ferric citrate in Japan (the License Deliverable), (ii) supply of ferric citrate until JT and Torii could secure their own source (the Supply Deliverable), (iii) knowledge transfer, and (iv) rights to future know-how.

The Company has identified two performance obligations in connection with its obligations under the JT and Torii Sublicense Agreement.

(i) License and Supply Performance Obligation

The License Deliverable does is not distinct from the Supply Deliverable. More specifically, JT and Torii was unable to manufacture ferric citrate at the onset of the agreement as it had not secured a source for this manufacturing. This significantly limits the ability for JT and Torii to use the license for their intended use in a way that generates economic benefits.

The License Deliverable does is not distinct from the knowledge transfer because JT and Torii cannot fully utilize the license for its intended purpose without the corresponding information regarding know-how, development data and regulatory materials possessed by the Company.

The License Deliverable does is not distinct from the supply or knowledge transfer. As a result, the License Deliverable, supply, and knowledge transfer do not qualify for separation and have been combined as a single performance obligation (the License Supply Performance Obligation).

(ii) Rights to Future Know-How Performance Obligation

The License and Supply Deliverables combined are distinct from the rights to future know-how because JT and Torii can obtain the value of the License and Supply Deliverables without receipt of any rights to future know-how that may be discovered or developed in the future. As a result, the rights to future know-how qualify for separation from the License and Supply Performance Obligation.

The Company allocates the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of the standalone selling price for the Rights to Future Know-How Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement and determined it immaterial. As such, the Company did not develop a best estimate of standalone selling price for the License and Supply Performance Obligation and allocated the entire transaction price to this performance obligation. Additionally, as of the consummation of the Merger, the services associated with the License and Supply Performance Obligation were completed and JT and Torii had secured their own source to manufacture ferric citrate. As such, any initial license fees as well as any development-based milestones and manufacturing fee revenue were received and recognized prior to the Merger. The Company determined that the remaining consideration that may be payable to the Company under the terms of the sublicense agreement are either quarterly royalties on net sales or payments due upon the achievement of sales-based milestones. In accordance with ASC 606, the Company recognizes sales-based royalties, including milestone payments based on the level of sales, when the related sales occur as these amounts

have been determined to relate predominantly to the license granted to JT and Torii and therefore are recognized at the later of when the performance obligation is satisfied, or the related sales occur.

During the period from December 12, 2018 to December 31, 2018, the Company recognized $0.1 million in license revenue related to royalties earned on net sales of ferric citrate in Japan. The Company records the associated mid-single digit percentage of net sales royalty expense due to Panion, the licensor of ferric citrate, in the same period as the royalty revenue from JT and Torii is recorded.

5. Business Combination

On December 12, 2018, the Company completed the Merger with Keryx. Keryx, headquartered in Boston, Massachusetts, is focused on the development and commercialization of medicines for people with kidney disease. Keryx's proprietary product, Auryxia® (ferric citrate) tablets, is approved by the U.S. Food and Drug Administration, or FDA, for two indications: (1) the control of serum phosphorus levels in adult patients with chronic kidney disease on dialysis and (2) the treatment of iron deficiency anemia in adult patients with chronic kidney disease not on dialysis.

Akebia has been determined to be the accounting acquirer and has accounted for the transaction as a business combination using the acquisition method of accounting under ASC 805. Accordingly, the results of Keryx's operations are included in our consolidated financial statements from December 12, 2018, the date the Merger was completed. Keryx's revenues and net loss from December 12, 2018 to December 31, 2018 were $6.9 million and $3.8 million, respectively.

Pursuant to the terms and conditions of the Merger Agreement, each outstanding share of Keryx common stock, excluding the Baupost Additional Shares discussed below, and each outstanding Keryx equity award were converted into Akebia common stock and substantially similar Akebia awards, respectively, at an exchange ratio of 0.37433 for a total fair value consideration of $527.8 million consisting of the following (in thousands):

| | |
|---|---|
| Fair value of 57,773,090 shares of Akebia common stock | $516,492 |
| Fair value of 602,752 Akebia RSUs | 304 |
| Fair value of 3,967,290 Akebia stock options | 10,958 |
| Total consideration | $527,754 |

The fair value of the Akebia common stock and Akebia awards issued was calculated using $8.94 per share, the closing price of Akebia common stock on December 12, 2018. The portion of the fair value relating to the Akebia RSUs and stock options represents the fair value attributable to precombination employee services. The fair value relating to future employee service will be expensed as stock-based compensation on a straight-line basis over the remaining service periods of those awards.

Additionally, immediately prior to the Merger, Baupost agreed to convert its $164.7 million of Keryx's Convertible Notes into 35,582,335 Keryx Shares, in accordance with the terms of the governing indenture agreement, in exchange for an additional 4,000,000 Keryx Shares (the "Baupost Additional Shares"). The aggregate 39.6 million Keryx Shares were then converted into Akebia shares at the 0.37433 exchange ratio. The fair value of the Baupost Additional Shares, on an as-converted bases, of $13.4 million has been excluded from the purchase price and recorded within general and administrative expenses in our consolidated financial statements, as the issuance of those shares by Keryx is considered to be a separate transaction under ASC 805 since it was entered into by or on behalf of the acquirer or primarily for the benefit of the acquirer or the combined entity.

The Company has allocated the $527.8 million purchase price to the identifiable assets acquired and liabilities assumed in the business combination at their fair values as of December 12, 2018 as follows (in thousands):

| | | |
|---|---|---|
| Cash and cash equivalents | $ | 5,257 |
| Inventory | | 235,597 |

| | | |
|---|---|---|
| Trade accounts receivable, net | 15,834 | |
| Prepaid expenses and other current assets | 8,399 | |
| Goodwill | 55,053 | |
| Intangible assets: | | |
| Developed product rights for Auryxia | 329,130 | |
| Other intangible assets | 545 | |
| Property and equipment, net | 3,646 | |
| Other assets | 14,441 | |
| Accounts payable | (17,570 | ) |
| Accrued expenses | (42,972 | ) |
| Deferred tax liability | (35,096 | ) |
| Debt | (15,000 | ) |
| Fair value of unfavorable executory contract | (29,510 | ) |
| Total purchase price | $ 527,754 | |

In performing the purchase price allocation, the Company considered, among other factors, the intended future use of acquired assets, analysis of historical financial performance and estimates of future performance of Keryx's business.

As part of the purchase price allocation, the Company identified developed product rights for Auryxia as the primary intangible asset. The fair value of the developed product rights for Auryxia is determined using the multi-period excess earnings method which is a variation of the income approach, and is a valuation technique that provides an estimate of the fair value of an asset based on the principle that the value of an intangible asset is equal to the present value of the incremental after-tax cash flows attributable to the asset, after taking charges for the use of other assets employed by the business. Key estimates and assumptions used in this model are projected revenues and expenses related to the asset, estimated contributory asset charges, and a risk-adjusted discount rate of 20.0% used to calculate the present value of the future expected cash inflows from the asset. The intangible asset will be amortized over its estimated useful life, which for Auryxia is 9 years.

The Company also identified an executory contract in the supply agreement between Keryx and BioVectra Inc., or BioVectra, which includes future firm purchase commitments. This executory contract was deemed to have an off-market element related to the amount of purchase commitments that exceed the current forecast and as such, the Company recorded a liability in purchase accounting. As of the acquisition date, the preliminary fair value of the off-market element was $29.5 million.

The preliminary goodwill represents the excess of the purchase price over the estimated fair value of net assets acquired. The factors contributing to the recognition of goodwill were based on several strategic and synergistic benefits that were expected to be realized from the Merger. These benefits included the expectation that the combined company would establish itself as a leading renal company with enhanced position and large market opportunity, synergistic utilization of Keryx's commercial organization, and strengthening the combined company's financial profile. Such goodwill is not deductible for tax purposes.

In connection with the Merger, the Company identified a preliminary deferred tax liability of $35.1 million as a result of the difference in the book basis and tax basis related to the identifiable inventory, other intangible assets, net and other liability. In determining the deferred tax liability to be recorded the Company elected to first consider the recoverability of the deferred tax assets acquired in the acquisition before considering the recoverability of the acquirer's existing deferred tax assets. The deferred tax liability recorded as part of purchase accounting creates a source of future income against which the Company can benefit it's tax attributes. The use of the Company's tax attributes resulted in a release of the corresponding valuation allowance which was recorded as a benefit in the statement of operations. The fair values of deferred taxes may be subject to change as additional information becomes known and certain tax returns are finalized. Accordingly, the purchase price allocation is preliminary and remains subject to potential adjustments for the finalization of income taxes relating to purchase accounting. There can be no assurance that such finalizations will not result in material changes from the preliminary purchase price allocation. The Company's estimates and assumptions are subject to change during the measurement period, which is up to one year from the acquisition date, as the Company finalizes the valuations of assets acquired and liabilities assumed.

In connection with the Merger, the Company incurred $23.1 million of direct transaction costs, which along with the expense associated with the Baupost Additional Shares, is recorded within general and administrative expenses in our consolidated financial statements for the year ended December 31, 2018.

The unaudited estimated pro forma results presented below include the effects of the Merger as if it had been consummated as of January 1, 2017. The non-recurring charges attributed to the Merger and incurred in 2018 include $13.4 million of expense associated with the Baupost Additional Shares, $39.5 million of acquisition-related costs, $10.4 million of stock-based compensation expenses as a result of the change in control, $4.5 million of bonus and severance payments, and $35.1 million of tax benefits. These expenses are included in the Company's historical income statement for the year ended December 31, 2018 and are reflected in pro forma earnings for the year ended December 31, 2017. The pro forma results include the amortization expense related to the fair value of the acquired intangible asset associated with the Auryxia developed product rights, a favorable office lease intangible asset, the

impact of a step-up in inventory, incremental stock-based compensation and rent expense. The pro forma results exclude the amortization of debt discount associated with Keryx's Convertible Notes. In addition, the pro forma results do not include any anticipated synergies or other expected benefits of the Merger. Accordingly, the unaudited estimated pro forma financial information below is not necessarily indicative of what the actual results of operations of the combined companies would have been had the acquisition occurred as of January 1, 2017, nor are they indicative of future results of operations:

| | For the Year Ended December 31, | |
|---|---|---|
| | 2018 | 2017 |
| | (in thousands) | |
| Total revenue | $305,822 | $240,125 |
| Net loss | $(322,664) | $(331,118) |
| Net loss per share, basic and diluted | $(2.75) | $(3.22) |

6. Available for Sale Securities

Available for sale securities at December 31, 2018 and 2017 consist of the following:

| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Fair Value |
|---|---|---|---|---|
| | (in thousands) | | | |
| December 31, 2018 | | | | |
| Cash and cash equivalents | $104,644 | $ — | $ — | $104,644 |
| Available for sale securities: | | | | |
| Certificates of deposit | $245 | — | — | $245 |
| U.S. government debt securities | 158,518 | 1 | (198) | 158,321 |
| Corporate debt securities | 58,494 | — | (64) | 58,430 |
| Total available for sale securities | $217,257 | $ 1 | $ (262) | $216,996 |
| Total cash, cash equivalents, and available for sale securities | $321,901 | $ 1 | $ (262) | $321,640 |

| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Fair Value |
|---|---|---|---|---|
| | (in thousands) | | | |
| December 31, 2017 | | | | |
| Cash and cash equivalents | $70,156 | $ — | $ — | $70,156 |
| Available for sale securities: | | | | |
| Certificates of deposit | $14,117 | — | — | $14,117 |
| U.S. government debt securities | 175,155 | — | (352) | 174,803 |
| Corporate debt securities | 58,806 | — | (90) | 58,716 |
| Total available for sale securities | $248,078 | $ — | $ (442) | $247,636 |
| Total cash, cash equivalents, and available for sale securities | $318,234 | $ — | $ (442) | $317,792 |

The estimated fair value of the Company’s available for sale securities balance at December 31, 2018, by contractual maturity, is as follows (in thousands):

| | |
|---|---|
| Due in one year or less | $216,751 |
| Due after one year | 245 |
| Total available for sale securities | $216,996 |

There were no realized gains or losses on available for sale securities for the years ended December 31, 2018 or 2017. The following table summarizes the Company’s available for sale securities that were in a continuous unrealized loss position, but were not deemed to be other-than-temporarily impaired, as of December 31, 2018 and 2017:

| | Unrealized Loss for Less Than 12 Months | | Unrealized Loss for 12 Months or More | | Total | |
|---|---|---|---|---|---|---|
| | Gross Unrealized Losses | Estimated Fair Value | Gross Unrealized Losses | Estimated Fair Value | Gross Unrealized Losses | Estimated Fair Value |
| | (in thousands) | | | | | |
| December 31, 2018 | | | | | | |
| Available for sale securities: | | | | | | |
| U.S. government debt securities | $(159) | $116,026 | $(39) | $29,934 | $(198) | $145,960 |
| Corporate debt securities | (64) | 58,430 | — | — | (64) | 58,430 |
| Total | $(223) | $174,456 | $(39) | $29,934 | $(262) | $204,390 |

| | Unrealized Loss for Less Than 12 Months | | Unrealized Loss for 12 Months or More | | Total | |
|---|---|---|---|---|---|---|
| | Gross Unrealized Losses | Estimated Fair Value | Gross Unrealized Losses | Estimated Fair Value | Gross Unrealized Losses | Estimated Fair Value |
| | (in thousands) | | | | | |
| December 31, 2017 | | | | | | |
| Available for sale securities: | | | | | | |
| U.S. government debt securities | $(343) | $170,812 | $(9) | $ 3,991 | $(352) | $174,803 |
| Corporate debt securities | (90) | 58,716 | — | — | (90) | 58,716 |
| Total | $(433) | $229,528 | $(9) | $ 3,991 | $(442) | $233,519 |

There were 51 securities and 60 securities as of December 31, 2018 and 2017, respectively, that were in an unrealized loss position. The Company considered the decline in the market value of these securities to be primarily attributable to current economic conditions. The contractual terms of these securities do not permit the issuer to settle the securities at a price less than the amortized cost basis of the investment. As of December 31, 2018, the Company does not intend to sell these securities and it was not more likely than not that the Company would be required to sell these securities before the recovery of their amortized cost basis, which may be at maturity. As a result, the Company did not consider these investments to be other-than-temporarily impaired as of December 31, 2018.

7. Fair Value of Financial Instruments

The Company utilizes a portfolio management company for the valuation of the majority of its investments. This company is an independent, third-party vendor recognized to be an industry leader with access to market information that obtains or computes fair market values from quoted market prices, pricing for similar securities, recently executed transactions, cash flow models with yield curves and other pricing models. For valuations obtained from the pricing service, the Company performs due diligence to understand how the valuation was calculated or derived, focusing on the valuation technique used and the nature of the inputs.

Based on the fair value hierarchy, the Company classifies its cash equivalents and available for sale securities within Level 1 or Level 2. This is because the Company values its cash equivalents and available for sale securities using quoted market prices or alternative pricing sources and models utilizing market observable inputs.

Assets measured or disclosed at fair value on a recurring basis as of December 31, 2018 and December 31, 2017 are summarized below:

| | Fair Value Measurements Using | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| | (in thousands) | | | |
| December 31, 2018 | | | | |

| | | | | |
|---|---|---|---|---|
| Assets: | | | | |
| Cash and cash equivalents | $104,644 | $— | $ — | $104,644 |
| Certificates of deposit | — | 245 | — | 245 |
| U.S. government debt securities | — | 158,321 | — | 158,321 |
| Corporate debt securities | — | 58,430 | — | 58,430 |
| | $104,644 | $216,996 | $ — | $321,640 |

| | Fair Value Measurements Using | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| | (in thousands) | | | |
| December 31, 2017 | | | | |
| Assets: | | | | |
| Cash and cash equivalents | $70,156 | $— | $ — | $70,156 |
| Certificates of deposit | — | 14,117 | — | 14,117 |
| U.S. government debt securities | — | 174,803 | — | 174,803 |
| Corporate debt securities | — | 58,716 | — | 58,716 |
| | $70,156 | $247,636 | $ — | $317,792 |

The Company’s corporate debt securities are all investment grade.

The Company had no assets or liabilities measured at fair value on a recurring basis using significant unobservable inputs (Level 3) at December 31, 2018 and December 31, 2017.

Investment securities are exposed to various risks such as interest rate, market and credit. Due to the level of risk associated with certain investment securities and the level of uncertainty related to changes in the value of investment securities, it is at least reasonably possible that changes in risks in the near term would result in material changes in the fair value of investments.

8. Inventory

The components of inventory are summarized as follows:

| | December 31, 2018 (in thousands) |
|---|---|
| Raw materials | $ 1,880 |
| Work in process | 215,122 |
| Finished goods | 18,182 |
| Total inventory | $ 235,184 |

| | December 31, 2018 (in thousands) |
|---|---|
| Balance Sheet Classification: | |
| Inventory | $ 114,245 |
| Other assets | 120,939 |
| Total inventory | $ 235,184 |

Long-term inventory, which primarily consists of raw materials and work in process, is included in other assets in the Company’s consolidated balance sheets.

There were no inventory amounts written down as a result of excess, obsolescence, scrap or other reasons that would be charged to cost of sales during the period from December 12, 2018 through December 31, 2018. If future sales of Auryxia are lower than expected, the Company may be required to write-down the value of such inventories. Inventory write-downs and losses on purchase commitments are recorded as a component of cost of sales in the consolidated statement of operations.

9. Intangible Assets and Goodwill

Intangible Assets

The following table presents the Company’s intangible assets:

| | December 31, 2018 (in thousands) | Estimated useful life |
|---|---|---|
| Intangible assets: | | |
| Developed product rights for Auryxia | $ 329,130 | 9 Years |
| Other intangible assets | 545 | 4 Years |
| | 329,675 | |
| Less accumulated amortization | (1,522) | |
| Total intangible assets, net | $ 328,153 | |

On December 12, 2018, the Company completed the Merger, whereby it acquired certain definite-lived intangible assets, including the developed product rights for Auryxia. The Company recorded $1.5 million in amortization expense related to intangible assets using the straight-line method, which is considered the best estimate of economic benefit, during the year ended December 31, 2018. Estimated future amortization expense for intangible assets as of December 31, 2018 is as follows:

| | Total |
|---|---|
| 2019 | $36,531 |
| 2020 | 36,531 |
| 2021 | 36,531 |
| 2022 | 36,531 |
| 2023 | 36,423 |
| Thereafter | 145,606 |
| | $328,153 |

Goodwill

As of December 31, 2018, the Company had goodwill of $55.1 million, generated from the Merger, in its consolidated balance sheet. Goodwill will be evaluated for impairment on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that an impairment may exist.

10. Accrued Expenses

Accrued expenses are as follows:

| | December 31, 2018 | December 31, 2017 |
|---|---|---|
| | (in thousands) | |
| Accrued clinical | $71,881 | $ 43,297 |
| Product revenue allowances | 22,861 | — |
| Merger costs | 16,071 | — |
| Accrued bonus | 9,537 | 3,388 |
| Accrued commercial manufacturing | 6,383 | — |
| Accrued severance | 3,962 | — |
| Royalties | 2,430 | — |
| Professional fees | 2,367 | 808 |
| Accrued payroll | 2,255 | 795 |
| Accrued vacation | 1,088 | 797 |
| Income tax payable | — | 987 |
| Accrued other | 12,082 | 2,369 |
| Total accrued expenses | $150,917 | $ 52,441 |

11. Debt

Revolving Line of Credit

Keryx, our wholly owned subsidiary following the Merger, has a $40.0 million revolving line of credit, or the Line of Credit, under its Loan and Security Agreement with Silicon Valley Bank, or SVB. Availability under the Line of Credit is subject to a borrowing base comprised of eligible receivables and eligible inventory as set forth in the Loan and Security Agreement. As of December 31, 2018, the Company had approximately $16.0 million in available borrowing base under the Revolving Loan Facility, of which $15.0 million is outstanding. Proceeds from the Line of Credit may be used for working capital and general business purposes. The Line of Credit is secured by substantially all of Keryx's assets other than its intellectual property. The Line of Credit restricts Keryx's ability to grant any interest in its intellectual property other than certain permitted licenses and permitted encumbrances set forth in the Loan and Security Agreement.

The principal amount outstanding under the Loan and Security Agreement bears interest at a floating rate per annum equal to the greater of (i) 2.0% above the "prime rate," as reported in The Wall Street Journal and (ii) 6.75%, which interest is payable monthly. Principal amounts borrowed under the Line of Credit may be repaid and, prior to the maturity date, re-borrowed, subject to the terms and conditions set forth in the Loan and Security Agreement. The Line of Credit matures on the date that is the earlier of (i) two years after the effective date of the Loan and Security Agreement and (ii) ninety days prior to the maturity of any portion of any Permitted Convertible Debt, as defined under the Loan and Security Agreement. Upon entry into the Loan and Security Agreement (payable in installments and subject to certain conditions), and at the one year anniversary of the effective date of the Loan and Security Agreement (or, if earlier, upon termination of or an event of default under the Loan and Security Agreement), Keryx must pay to SVB a fee equal to 1.00% of the Line of Credit. Keryx is also required to pay on a quarterly basis a fee equal to 0.25% per annum of the average unused portion of the Line of Credit. Keryx must pay a termination fee of 2.00% of the Line of Credit, if the Loan and Security Agreement is terminated prior to the maturity date, subject to certain exceptions.

The Loan and Security Agreement contains customary covenants applicable to Keryx and its subsidiaries, including maintaining insurance on its business, achievement of minimum revenue amounts, the incurrence of additional indebtedness, and future encumbrances on Keryx's assets. In addition, the Keryx must maintain a liquidity ratio, defined as (i) the sum of unrestricted and unencumbered cash and cash equivalents maintained at SVB or its affiliates plus net billed accounts receivable divided by (ii) all outstanding obligations and liabilities of Keryx to SVB, including the aggregate amount of Keryx's obligations to SVB under any business credit cards, of at least 1.5 to 1.0, measured monthly.

Upon an event of default under the Loan and Security Agreement, SVB is entitled to accelerate and demand payment of all amounts outstanding under the Loan and Security Agreement, stop advancing money or extending credit to Keryx, demand that Keryx deposit at least 105% of the face amount of any letters of credit remaining undrawn to secure all obligations thereunder, and exercise other remedies available to SVB under the Loan and Security Agreement and at law or in equity. As of December 31, 2018, the Company has determined that events of default have already occurred, and has not obtained a formal waiver from SVB with respect to these events of default. As a result, the Company has classified the outstanding principal of $15.0 million as a current liability in its consolidated balance sheet as of December 31, 2018. So long as these events of default are not waived or otherwise resolved, SVB has the right to take any of the foregoing remedies. If SVB were to accelerate all of the obligations outstanding under the Loan and Security Agreement, the Company would be required to pay the outstanding principal and other fees to SVB, and the Company would no longer have access to the Line of Credit. These events of default have no impact on the Company's liquidity, as the Company's operating plan and cash forecast assumes the payment of all amounts due to SVB and no future borrowings under the Line of Credit.

During the period from December 12, 2018 through December 31, 2018, the Company recognized approximately $65,000 of interest expense related to the Line of Credit. The Company did not incur any amortization expense related to the origination fee and other additional fees noted above as such fees were included in the fair value of the Line of Credit as of December 12, 2018, the date of which the Merger was consummated, in accordance with ASC 805.

12. Warrant

In connection with the Janssen Agreement, in February 2017, the Company issued a warrant to purchase 509,611 shares of the Company's common stock at an exercise price of $9.81 per share. The warrant was fully vested upon issuance and exercisable in whole or in part, at any time prior to February 9, 2022. The warrant satisfied the equity classification criteria of ASC 815, and is therefore classified as an equity instrument. The fair value at issuance of $3.4

million was calculated using the Black-Scholes option pricing model and was charged to research and development expense as it represented consideration for a license for which the underlying intellectual property was deemed to have no alternative future use. As of December 31, 2018, the warrant remains outstanding and expires on February 9, 2022.

13. Stockholders' Equity

Authorized and Outstanding Capital Stock

As of December 31, 2018, the authorized capital stock of the Company included 175,000,000 shares of common stock, par value $0.00001 per share, of which 116,887,518 and 47,612,619 shares were issued and outstanding at December 31, 2018 and 2017, respectively; and 25,000,000 shares of undesignated preferred stock, par value $0.00001 per share, of which 0 shares were issued and outstanding at December 31, 2018 and December 31, 2017.

At-the-Market Facility

In May 2016, the Company established an at-the-market, or ATM, equity offering program pursuant to which it was able to offer and sell up to $75.0 million its common stock at the then current market prices from time to time. In September 2016, the Company commenced sales under this program. Through December 31, 2017, the Company sold 1,080,908 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $12.1 million. Additionally, the Company sold 694,306 shares in the three months ended March 31, 2018 for net proceeds (after deducting commissions and other offering expenses) of approximately $10.5 million. The Company has not sold any additional shares under this program subsequent to March 31, 2018.

Equity Offering

In March 2018, the Company completed a follow-on public equity offering, whereby the Company sold 8,500,000 shares of common stock at a public offering price of $10.50 per share. The aggregate net proceeds received by the Company from the offering were approximately $84.8 million, net of underwriting discounts and commissions and estimated offering expenses payable by the Company.

Shares Issued and Awards Assumed in Connection with Business Combination

On December 12, 2018, the Company completed the Merger. Pursuant to the terms and conditions of the Merger Agreement, each Keryx Share issued and outstanding as of the Effective Time was cancelled and converted into 0.37433 fully paid and non-assessable Akebia Shares. As a result, in December 2018, the Company issued 57,773,090 shares of common stock to Keryx shareholders, and 1,497,320 shares issued as part of the Baupost Additional Shares which has been excluded from the business combination purchase price (see Note 5).

Additionally, in connection with the Merger, the Company converted outstanding and unexercised options to purchase Keryx Shares into 3,967,290 options to purchase Akebia Shares, as adjusted to the reflect the Exchange Multiplier, of which 3,733,336 are service-based stock options and 233,954 are performance-based stock options. The Company also converted outstanding Keryx Restricted Shares into 602,752 Akebia RSUs, of which 486,709 are service-based RSUs and 116,043 are performance-based RSUs.

Acceleration of Equity Awards

In connection with the closing of the Merger, certain executives of Keryx were terminated and as a result, the Company accelerated in full the vesting of all of the outstanding equity awards for each such executive, consistent with his or her existing employment agreements. Additionally, subject to limited exceptions, all outstanding equity awards held by certain officers of Akebia also had the vesting of their outstanding equity awards accelerated in full upon consummation of the Merger as a result of the change in control provision included in each such officer’s award agreements and their Executive Severance Agreements. As a result, the Company recognized $9.7 million of stock-based compensation expense related to the acceleration of awards.

Equity Plans

On February 28, 2014, the Company’s Board of Directors adopted its 2014 Incentive Plan and its 2014 Employee Stock Purchase Plan, or the ESPP, which were subsequently approved by its shareholders and became effective upon the closing of the Company’s initial public offering on March 25, 2014. The Company’s 2014 Incentive Plan was subsequently amended on December 11, 2018, which amendment did not require shareholder approval. The Company’s 2014 Incentive Plan, as amended, is referred to as the 2014 Plan. The 2014 Plan replaced the Company’s Amended and Restated 2008 Equity Incentive Plan, the 2008 Plan; however, options or other awards granted under

the 2008 Plan prior to the adoption of the 2014 Plan that have not been settled or forfeited remain outstanding and effective. In May 2016 the Company's Board of Directors approved an inducement award program that was separate from the Company's equity plans and which, consistent with Nasdaq Listing Rule 5635(c)(4), did not require shareholder approval, or the Inducement Award Program. For 2018, the Company authorized the issuance of up to 750,000 shares for the purpose of granting options to purchase shares of the Company's common stock to new hires under the Inducement Award Program, of which 375,750 options to purchase shares of the Company's common stock were granted during the year. At December 31, 2018, 349,374 options granted in 2018 under the Inducement Award Program remain outstanding.

The 2014 Plan allows for the granting of stock options, stock appreciation rights, or SARs, restricted stock, unrestricted stock, RSUs, performance awards and other awards convertible into or otherwise based on shares of the Company's common stock. Dividend equivalents may also be provided in connection with an award under the 2014 Plan. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2014 Plan. The Company initially reserved 1,785,000 shares of its common stock for the issuance of awards under the 2014 Plan. The 2014 Plan provides that the number of shares reserved and available for issuance under the 2014 Plan will automatically increase annually on January 1st of each calendar year, by an amount equal to three percent (3%) of the number of shares of the Company's common stock outstanding on a fully diluted basis as of the close of business on the immediately preceding December 31st, or the 2014 Plan Evergreen Provision. The Company's Board of Directors may act prior to January 1st of any year to provide that there will be no automatic increase in the number of shares available for grant under the 2014 Plan for that year (or that the increase will be less than the amount that would otherwise have automatically been made). On December 12, 2018, in connection with the consummation of the Merger, the Company assumed outstanding and unexercised options to purchase Keryx Shares, as adjusted by the Exchange Multiplier pursuant to the terms of the Merger Agreement, under the following Keryx equity plans, or the Keryx Equity Plans: the Keryx 1999 Share Option Plan, the Keryx 2004 Long-Term Incentive Plan, the Keryx 2007 Incentive Plan, the Keryx Amended and Restated 2013 Incentive Plan, and the Keryx 2018 Equity Incentive Plan, or the Keryx 2018 Plan. In addition, the number of Keryx Shares available for issuance under the Keryx 2018 Plan, as adjusted by the Exchange Multiplier pursuant to the terms of the Merger Agreement, may be used for awards by the Company under its 2014 Plan, or the Assumed Shares, provided that the Company uses the Assumed Shares for individuals who were not employees or directors of the Company prior to the consummation of the Merger. During the year ended December 31, 2018, the Company granted 862,148 options to purchase Akebia Shares to employees under the 2014 Plan, 375,750 options to purchase Akebia Shares to employees under the Inducement Award Program, 644,340 Akebia RSUs to employees under the 2014 Plan, and 262,500 options to purchase Akebia Shares to directors under the 2014 Plan. Additionally, as noted above, the Company assumed 3,967,290 options and issued 602,752 Akebia RSUs in connection with the Merger.

The ESPP provides for the issuance of options to purchase shares of the Company's common stock to participating employees at a discount to their fair market value. The maximum aggregate number of shares of the Company's common stock available for purchase pursuant to the exercise of options granted under the ESPP will be the lesser of (a) 262,500 shares, increased on each anniversary of the adoption of the ESPP by one percent (1%) of the total shares of common stock then outstanding, the ESPP Evergreen Provision, and (b) 739,611 shares, which is equal to five percent (5%) of the total shares of common stock outstanding on the date of the adoption of the ESPP on a fully diluted, as converted basis. Under the ESPP, each offering period is six months, at the end of which employees may purchase shares of the Company's common stock through payroll deductions made over the term of the offering. The per-share purchase price at the end of each offering period is equal to the lesser of eighty-five percent (85%) of the closing price of the Company's common stock at the beginning or end of the offering period.

Shares Reserved for Future Issuance

The Company has reserved for future issuance the following number of shares of common stock:

| | December 31, 2018 | December 31, 2017 |
|---|---|---|
| Common stock options and RSUs outstanding [1] | 9,309,204 | 4,388,752 |
| Shares available for issuance under the 2014 Plan [2] | 4,526,563 | 1,790,600 |
| Warrant to purchase common stock | 509,611 | 509,611 |
| Shares available for issuance under the ESPP [3] | 603,522 | 652,290 |

| | | |
|---|---|---|
| Total | 14,948,900 | 7,341,253 |

(1) Includes awards granted under the 2014 Plan and the Inducement Award Program and awards issued in connection with the Merger.

(2) On January 1, 2019, January 1, 2018 and January 1, 2017, the shares reserved for future grants under the 2014 Plan increased by 3,801,198, 1,575,329 and 1,265,863 shares, respectively, pursuant to the 2014 Plan Evergreen Provision. On December 12, 2018, the shares reserved for future grants under the 2014 Plan increased by 2,323,213 shares as a result of the Company's addition of the Assumed Shares to the 2014 Plan. On December 19, 2017, the Company's Board of Directors approved 750,000 shares for issuance as option awards in fiscal year 2018 under the Inducement Award Program. Additionally, on January 30, 2019, the Company's Board of Directors approved 3,150,000 shares for issuance as option awards in fiscal year 2019 under the Inducement Award Program, or the 2019 Inducement Shares. As the 2019 Inducement Shares were not available for issuance as of December 31, 2018, they have been excluded from the table above.

(3) On February 28, 2018 and February 28, 2017, the shares reserved for future issuance under the ESPP remained unchanged. There were no increases in the shares reserved for future issuance pursuant to the ESPP Evergreen Provision subsequent to February 28, 2016 as the maximum aggregate number of shares available for purchase had reached its cap of 739,611.

Stock-Based Compensation

Stock Options

Service-Based Stock Options

On February 28, 2018, as part of the Company's annual grant of equity, the Company issued 522,200 stock options to employees. In addition, the Company issues stock options to directors, new hires and occasionally to other employees not in connection with the annual grant process. Options granted by the Company vest over periods of between 12 and 48 months, subject, in each case, to the individual's continued service through the applicable vesting date. Options vest either 100% on the first anniversary of the grant date or in installments of (i) 25% at the one year anniversary and (ii) 12 equal quarterly installments beginning after the one year anniversary of the grant date, subject to the individual's continuous service with the Company. Options generally expire ten years after the date of grant. The Company recorded approximately $11.9 million, $6.5 million and $4.7 million of stock-based compensation expense related to stock options granted during fiscal years 2018, 2017 and 2016, respectively.

On December 12, 2018, pursuant to the Merger Agreement, each outstanding and unexercised option to acquire Keryx Shares granted under a Keryx equity plan converted into an option to acquire Akebia Shares, with the number of shares and exercise price adjusted by the Exchange Multiplier. As a result, the Company assumed 3,733,336 service-based options related to the Merger. The vesting schedule for these options is consistent with the vesting schedule noted above. The Company recorded approximately $0.2 million of stock-based compensation expense related to stock options assumed in 2018.

The assumptions used in the Black-Scholes pricing model to estimate the grant date fair value of options granted under the 2014 Plan are as follows:

| | Year ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Risk-free interest rate | 2.54% - 3.01% | 1.81% - 2.27% | 1.16% - 2.03% |
| Dividend yield | 0.00% | 0.00% | 0.00% |
| Volatility | 61.65% - 77.04% | 78.57% - 85.81% | 64.78% - 82.40% |
| Expected term (years) | 5.51 - 6.25 | 5.51 - 6.25 | 5.51 - 6.25 |

The following table summarizes the Company's stock option activity, excluding performance-based options, for the year ended December 31, 2018:

| | Shares | Weighted-Average Exercise Price | Weighted-Average Contractual Life (in years) | Aggregate Intrinsic Value |
|---|---|---|---|---|
| Outstanding, December 31, 2017 | 3,660,014 | $ 9.47 | | $21,932,858 |
| Granted | 1,500,398 | $ 10.72 | | |
| Assumed in connection with the Merger | 3,733,336 | $ 17.83 | | |

| | | | | | |
|---|---|---|---|---|---|
| Exercised | (178,382 ) | $ | 3.63 | | $1,222,914 |
| Forfeited | (570,614 ) | $ | 10.78 | | $1,171,979 |
| Expired/cancelled | — | $ | — | | |
| Outstanding, December 31, 2018 | 8,144,752 | $ | 13.57 | 7.44 | $2,351,316 |
| Options exercisable, December 31, 2018 | 6,423,555 | $ | 14.32 | 6.99 | $2,351,316 |
| Vested and expected to vest, December 31, 2018 | 8,144,752 | $ | 13.57 | | |

The weighted-average grant date fair values of options granted in the years ended December 31, 2018, 2017, and 2016 were $7.12, $8.47, and $5.22 per share, respectively. The total intrinsic value of options exercised during the years ended December 31, 2018, 2017, and 2016 were $1.2 million, $2.7 million, and $0.6 million, respectively. The fair value of options that vested during the years ended December 31, 2018, 2017, and 2016 were $13.6 million, $5.6 million, and $4.6 million, respectively. As of December 31, 2018, there was approximately $8.7 million of unrecognized compensation cost related to stock options under the Company’s 2014 Plan or made pursuant to the Inducement Award Program, which is expected to be recognized over a weighted average period of 2.86 years.

Performance-Based Stock Options

On December 12, 2018, pursuant to the Merger Agreement, each outstanding and unexercised performance-based option to acquire Keryx Shares granted under a Keryx equity plan converted into a service-based option or performance-based option to acquire Akebia Shares, with the number of shares and exercise price adjusted by the Exchange Multiplier. As a result, the Company issued 233,954 performance-based options related to the Merger. The Company did not have any performance based-options outstanding in fiscal year 2018 prior to the Merger. The potential range of shares issuable pursuant to the Company's performance-based options range from 0% to 100% of the target shares based on financial measures. Performance-based options vest up to 50% upon achievement of performance condition and up to 50% one year following achievement of the performance condition.

The following table summarizes the Company's performance-based option activity for the year ended December 31, 2018:

| | Shares | Weighted-Average Exercise Price | Weighted-Average Contractual Life (in years) | Aggregate Intrinsic Value |
|---|---|---|---|---|
| Outstanding, December 31, 2017 | — | $ — | | $ — |
| Granted | 233,954 | $ 18.96 | | |
| Exercised | — | $ — | | $ — |
| Forfeited/cancelled | (31,818 ) | $ 13.52 | | |
| Outstanding, December 31, 2018 | 202,136 | $ 19.82 | 7.42 | $ — |

The Company did not record any stock-based compensation expense related to performance-based options during 2018, 2017 and 2016. There were no performance-based options that vested during fiscal years 2018, 2017 or 2016. As of December 31, 2018, there was up to approximately $0.5 million of unrecognized compensation costs related to performance-based stock options under the Company's 2014 Plan, which if the performance conditions are achieved, is expected to be recognized in a 1.0 year period.

Restricted Stock

On December 23, 2013, the Company issued 450,224 shares of restricted stock to employees and 79,067 shares of restricted stock to non-employees at a grant date fair value of $7.42 per share. The aggregate grant date fair value for the shares of restricted stock issued on December 23, 2013 totaled approximately $3.9 million. The Company records stock-based compensation expense for restricted stock awards based on the grant date fair value for employees and the reporting date and upon vesting fair value for non-employees. The fair value of the award is considered the intrinsic value as of each measurement date. Compensation expense related to the restricted stock awards was being recognized over the associated requisite service period. The Company recorded approximately $0.2 million of stock-based compensation expense related to restricted stock during 2017. Restricted shares were fully vested as of December 31, 2017 and there were no additional grants of restricted stock during the year ended December 31, 2018, as such, there was no stock-based compensation expense related to restricted stock during the year ended December 31, 2018.

Restricted Stock Units

On February 28, 2018, as part of the Company's annual grant of equity, the Company issued 367,250 RSUs to employees. In addition, the Company occasionally issues RSUs not in connection with the annual grant process to employees. 100% of each RSU grant vests on either the first or the third anniversary of the grant date, subject, in each case, to the individual's continued service through the applicable vesting date. The expense recognized for these awards is based on the grant date fair value of the Company's common stock multiplied by the number of units granted and recognized on a straight-line basis over the vesting period. The Company recorded approximately $5.8 million, $2.0 million and $0.8 million of stock-based compensation expense related to the Akebia employee RSUs in 2018, 2017 and 2016, respectively.

On December 12, 2018, pursuant to the Merger Agreement, each Keryx Share that was subject to a Keryx restricted share award, other than those Keryx restricted shares that accelerated or lapsed as a result of the completion of the Merger, was converted into an RSU award of Akebia, covering the number of Akebia Shares determined in accordance with the Exchange Multiplier. As a result, the Company issued 486,709 service-based RSUs in substitution for Keryx restricted share awards in connection with the Merger. These RSUs vest either (i) in 3 equal annual installments beginning after the one-year anniversary of the grant date or (ii) one third on the one year anniversary of the grant date with the remaining RSUs vesting on the first day of each calendar quarter over the next two years thereafter. The Company recorded approximately $0.9 million of stock-based compensation expense related to RSUs issued in 2018 in substitution for the Keryx restricted share awards.

A following table summarizes the Company's RSU activity for the year ended December 31, 2018:

| | Shares | Weighted-Average Grant Date Fair Value |
|---|---|---|
| Unvested balance, December 31, 2017 | 728,738 | $ 9.26 |
| Granted | 644,340 | $ 11.22 |
| Issued in connection with the Merger | 486,709 | $ 8.94 |
| Vested | (818,395) | $ 10.40 |
| Forfeited | (195,119) | $ 10.58 |
| Outstanding, December 31, 2018 | 846,273 | $ 9.16 |

As of December 31, 2018, there was approximately $5.4 million of unrecognized compensation cost related to RSUs, which is expected to be recognized over a weighted average period of 2.2 years.

Employee Stock Purchase Plan

The first offering period under the ESPP opened on January 2, 2015. The Company issued 48,768 shares during the year ended December 31, 2018. The Company recorded approximately $0.2 million, $0.2 million and $0.1 million of stock-based compensation expense related to the ESPP during 2018, 2017 and 2016, respectively.

Compensation Expense Summary

The Company has recognized the following compensation cost related to share-based awards:

| | Years ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| | (in thousands) | | |
| Research and development | $5,755 | $6,496 | $2,136 |
| Selling, general and administrative | 13,285 | 5,784 | 3,689 |
| Total | $19,040 | $12,280 | $5,825 |

Compensation expense by type of award:

| | Years ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| | (in thousands) | | |
| Stock options | $12,114 | $6,512 | $4,674 |
| Restricted stock | — | 158 | 266 |
| Restricted stock units | 6,731 | 2,021 | 780 |
| Employee stock purchase plan | 195 | 176 | 105 |
| Warrant | — | 3,413 | — |
| Total | $19,040 | $12,280 | $5,825 |

Included in the compensation expense of stock options and RSUs for the year ended December 31, 2018, is approximately $1.1 million related to awards assumed under the Merger and acceleration of the vesting for awards of certain officers of Keryx.

14. Income Taxes

Effective January 1, 2018, (as noted in Note 2) the Company adopted ASC 606, using the full retrospective transition method. Under this method, the Company has revised its consolidated financial statements for the year ended December 31, 2017, and applicable interim periods within those years, as if ASC 606 had been effective for those periods. The adoption of this guidance did not have a significant impact on the Company’s related tax disclosures.

The Company's income tax provision was computed based on the federal statutory rate and the state statutory rates, net of the related federal benefit. There was no current or deferred income tax expense or benefit for the years ended December 31, 2017 and 2016 due to the Company's net losses and increases in its valuation allowance against its deferred tax assets. At December 31, 2018 the Company recorded a tax benefit of $28.3 million as a result of the Merger with Keryx. As part of purchase accounting, the Company recorded a deferred tax liability that is a source of income for which the Company can benefit from its tax attributes. The use of the Company's tax attributes resulted in a release of the corresponding valuation allowance associated with this benefit.

The provision for income taxes for each of the years ended December 31, 2018, 2017 and 2016 consisted of the following:

| | Year ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Current: | | | |
| Federal | 23 | — | — |
| State | 104 | — | — |
| Total Current: | 127 | — | — |
| Deferred: | | | |
| Federal | (16,383) | — | — |
| State | (12,082) | — | — |
| Total Deferred: | (28,465) | — | — |
| Total Income Taxes | (28,338) | — | — |

Our effective income tax rate differs from the statutory federal income tax rate as follows for the years ended December 31, 2018, 2017 and 2016:

| | Year ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Federal tax at statutory rate | 21.0 % | 34.0 % | 34.0 % |
| State and local tax at statutory rate | 4.1 | 3.8 | 1.4 |
| Research and development tax credits | 5.0 | 11.9 | 6.4 |
| Equity compensation | — | (0.6) | (0.2) |
| Alternative minimum tax | — | (1.3) | — |
| Change in valuation allowance | 16.3 | 6.9 | (41.6) |
| Impact of US tax reform | — | (54.7) | — |
| Non-Deductible Transaction Costs | (3.1) | — | — |
| Other Permanent Differences | (0.7) | — | — |
| Reduction in DTA for change in ownership | (26.1) | — | — |
| Effective tax rate | 16.5 % | 0.0 % | 0.0 % |

On December 22, 2017, "H.R.1," known as the Tax Cuts and Jobs Act, was signed into law. The Tax Cuts and Jobs Act, among other items, reduces the corporate income tax rate from 35% to 21%, effective January 1, 2018. As such, Akebia completed a revaluation of its net deferred tax assets. Akebia's deferred tax assets, net of deferred tax liabilities, represent expected corporate tax benefits anticipated to be realized in the future. The reduction in the federal corporate tax rate reduces these benefits.

For the year ended December 31, 2017, the Company evaluated the impact of the "Tax Cuts and Jobs Act," and determined that a reduction in its deferred tax asset of $43.0 million be recorded in the fourth quarter of 2017. However, the Company’s lack of earnings history and the uncertainty surrounding the Company’s ability to generate taxable income prior to the utilization of the deferred tax assets is completely offset by a valuation allowance. In 2018 the Company completed its review of the Tax Cuts and Jobs Act and has finalized adjustments related to its deferred tax assets and liabilities that resulted from the changes in the tax law.

For the year ended December 31, 2017, the Company had taxable income primarily due to timing differences. The income was fully offset with available net operating losses, or NOLs, for regular federal and state tax purposes. The Company did have a tax liability that was based on the Alternative Minimum Tax and resulted in approximately $0.8 million of Federal Tax, however due to tax reform, the amount is fully refundable through 2021 and thus the net result is that the Company recorded an income tax receivable of approximately $0.8 million rather than a tax expense for the year ended December 31, 2017.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. When realization of the deferred tax asset is more likely than not to occur, the benefit related to the deductible temporary differences attributable to operations is recognized as a reduction of income tax expense. Valuation allowances are provided against deferred tax assets when, based on all available evidence, it is considered more likely than not that some portion or all of the recorded deferred tax assets will not be realized in future periods. The Company cannot be certain that future taxable income will be sufficient to realize its deferred tax assets, and accordingly a valuation allowance has been provided on its deferred tax assets. The Company continues to maintain the underlying tax benefits to offset future taxable income and to monitor the need for a valuation allowance based on the profitability of its future operations. The valuation allowance increased by approximately $23.3 million and decreased by approximately $4.9 million, during the years ended December 31, 2018 and 2017, respectively. Significant components of the Company's deferred tax assets and liabilities are as follows:

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| | (in thousands) | |
| Deferred tax assets: | | |
| Accrued expenses | $4,993 | $4,305 |
| Deferred revenue | 28,533 | 32,093 |
| Intangible assets | — | 509 |
| Stock based compensation | 9,514 | 3,129 |
| Research and development credits | 2,899 | 25,322 |
| Other non-current liabilities | 7,567 | — |
| Net operating loss carryforward | 189,842 | 42,335 |
| Other | 853 | 600 |
| Total deferred tax assets | 244,201 | 108,293 |
| Less valuation allowance | (131,424) | (108,112) |
| Total deferred tax assets, net of valuation allowance | 112,777 | 181 |
| Deferred tax liabilities: | | |
| Fixed assets | (121) | (181) |
| Intangible Assets | (81,847) | — |
| Inventory | (37,440) | — |
| Total deferred tax liabilities | (119,408) | (181) |
| Net deferred tax liability | $(6,631) | $— |

At December 31, 2018 and 2017, the Company has approximately $0.6 million (after amortization of $1.3 million) and $0.8 million (after amortization of $1.1 million), respectively, of start-up expenses capitalized for income tax purposes with amortization available to offset future federal, state and local income tax.

As of December 31, 2018 and 2017, the Company has approximately $790.0 million and $179.7 million, respectively, of federal NOL carry-forwards which expire through 2037. Included in the $790.0 million of federal NOLs are losses of $208.0 million that will carry forward indefinitely as a result of the Tax Cuts and Jobs Act. Additionally, at December 31, 2018 and 2017, the Company has approximately $442.4 million and $74.6 million, respectively, of state NOL carry-forwards which expired through 2038. The Company also has approximately $3.7 million of state research and development tax credit carryforwards which expire through 2038.

Under the provisions of the Internal Revenue Code, the net operating losses and tax credit carry-forwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating losses and tax credit carryforwards may become subject to an annual limitation under Internal Revenue Code 382 and 383 if there is more than a 50% change in ownership of the stockholders that own 5% or more of the company's outstanding stock over a three-year period. The Company has completed an evaluation of its ownership changes and concluded that an ownership change did occur on December 12, 2018 for both Akebia and Keryx in connection with the Merger. As a consequence of this ownership change, the Company's NOL's and tax credit carryforwards allocable to the tax periods preceding the ownership change became subject to limitation under Section 382. The Company has reduced its associated deferred tax assets by $44.9 million as a result of the limitation.

The Company generated research credits but has not conducted a formal study to document its qualified activities. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carry-forwards and the valuation allowance.

The Company files income tax returns in the U.S. federal and various state and local jurisdictions. For federal and state income tax purposes, the 2017, 2016 and 2015 tax years remain open for examination under the normal three-year statute of limitations. The statute of limitations for income tax audits in the United States will commence upon utilization of net operating losses and will expire three years from the filing of the tax return the loss was utilized on.

There was no accrual for uncertain tax positions or for interest and penalties related to uncertain tax positions for 2018, 2017 and 2016. The Company does not believe that there will be a material change in its unrecognized tax positions over the next twelve months. All of the unrecognized tax benefits, if recognized, would be offset by the valuation allowance.

15. Employee Retirement Plan

During 2008, the Company established a retirement plan, or the Plan, authorized by Section 401(k) of the Internal Revenue Code. In accordance with the Plan, all employees who have attained the age of 21 are eligible to participate in the Plan as of the first Entry Date, as defined, following their date of employment. Each employee can contribute a percentage of compensation up to a maximum of the statutory limits per year. Company contributions are discretionary and contributions in the amount of approximately $0.3 million, $0.2 million and $0.2 million were made during the years ended December 31, 2018, 2017 and 2016, respectively.

16. Commitments and Contingencies

Leases

The Company leases approximately 65,167 square feet of office and lab space in Cambridge, Massachusetts under a lease which was most recently amended in April 2018, collectively the Cambridge Lease. Under the Third Amendment to the Cambridge Lease, or the Third Amendment, executed in July 2016, total monthly lease payments under the initial base rent were approximately $242,000 and are subject to annual rent escalations. In addition to such annual rent escalations, base rent payments for a portion of said premises commenced on January 1, 2017 in the monthly amount of approximately $22,000. The Fourth Amendment to the Cambridge Lease, executed in May 2017, provided additional storage space to the Company and did not impact rent payments. In April 2018, the Company entered into a Fifth Amendment to the Cambridge Lease, or the Fifth Amendment, for an additional 19,805 square feet of office space on the 12$^{th}$ floor. Monthly lease payments for the existing 45,362 square feet of office and lab space, under the Third Amendment, remain unchanged. The new space leased by the Company was delivered in September 2018 and additional monthly lease payments of approximately $135,000 will commence in February 2019 and are subject to annual rent escalations, commencing in September 2019.

Additionally, as a result of the Merger, the Company now has a lease for 27,300 square feet of office space in Boston, Massachusetts, or the Boston Lease, which expires in February 2023. The total monthly lease payments under the base rent are approximately $136,000 and are subject to annual rent escalations.

Committed landlord contributions included in the Cambridge Lease totaled $3,289,170, including $1,083,453 in leasehold improvements not yet utilized. The landlord contributions are being accounted for as a deferred lease incentive and reduction in monthly rent expense over the term of the lease. The term of the Cambridge Lease with respect to the office space expires on September 11, 2026, with one five year extension option available. The term of the Cambridge Lease with respect to the lab space expires on November 30, 2021, with an extension option for one additional period of two years. The term of the Boston Lease office space expires on February 28, 2023, with an extension option for one additional five year extension option available. Under the Fifth Amendment, the total security deposit in connection with the Cambridge Lease increased by $0.5 million from $1.3 million to $1.8 million.

In May 2018, the security deposit was reduced by $0.2 million to $1.6 million, which remains in effect as of December 31, 2018. Additionally, the Company recorded $0.8 million for the security deposit under the Boston Lease. Both the Cambridge Lease and the Boston Lease have their security deposits is in the form of a letter of credit, all of which are included in other assets in the Company's consolidated balance sheets as of December 31, 2018.

The Company recognizes rent expense for the space it currently occupies under the Cambridge Lease and records a deferred lease obligation representing the cumulative difference between actual facility lease payments and lease expense recognized ratably over the lease period, which is included in the Company's consolidated balance sheets as of December 31, 2018 and December 31, 2017.

At December 31, 2018, the Company's future minimum payments required under these leases are as follows:

| | Operating Lease (in thousands) |
|---|---|
| 2019 | $ 6,777 |
| 2020 | 7,008 |
| 2021 | 7,064 |
| 2022 | 6,735 |
| 2023 | 5,347 |
| Thereafter | 13,934 |
| Total | $ 46,865 |

The Company recorded approximately $3.7 million, $3.2 million and $2.5 million in rent expense for the years ended December 31, 2018, 2017 and 2016, respectively.

Manufacturing Agreements

As part of the Merger, the Company retained Keryx's commercial supply agreements with BioVectra Inc., or BioVectra, and Siegfried Evionnaz SA, or Siegfried, to supply commercial drug substance for Auryxia.

Pursuant to the BioVectra Manufacture and Supply Agreement and the Product Manufacture and Supply and Facility Construction Agreement, collectively the BioVectra Agreement, the Company has agreed to purchase a minimum quantity of drug substance of Auryxia at predetermined prices. The price per metric kilogram will decrease with an increase in quantity above the minimum purchase quantity. In addition, the BioVectra Agreement contained contingent milestone payments for capital developments in connection with construction of an expansion of the site of the BioVectra production facility for the manufacture of drug substance for Auryxia. These milestone payments were achieved by BioVectra and fully recorded prior to the Merger. These milestone payments are recorded in other assets and amortized into drug substance as inventory is released to the Company. The term of the BioVectra Agreement expires in late 2026, after which, it automatically renews for specified terms until terminated. The Company may terminate the BioVectra Agreement prior to the expiration of the contract term, which could result in early termination fee. As of December 31, 2018, the Company is required to purchase a minimum quantity of drug substance for Auryxia annually at a total cost of approximately $154.0 million through the end of the contract term.

As part of purchase accounting, the Company identified an executory contract in the supply agreement between Keryx and BioVectra, which includes future firm purchase commitments. This executory contract was deemed to have an off-market element related to the amount of purchase commitments that exceed the current forecast and as such, the Company recorded a liability in purchase accounting. As of the acquisition date, the preliminary fair value of the off-market element was $29.5 million

Pursuant to the Siegfried Master Manufacturing Services and Supply Agreement, or the Siegfried Agreement, the Company has agreed to purchase a minimum quantity of drug substance of Auryxia at predetermined prices. The price per metric kilogram will decrease with an increase in quantity above the minimum purchase quantity. The term of the Siegfried Agreement expires on December 31, 2021, after which, it automatically renews for one-year terms until terminated. The Siegfried Agreement provides for certain termination rights prior to December 31, 2021 for the

Company. As of December 31, 2018, the Company is required to purchase a minimum quantity of drug substance for Auryxia annually at a total cost of approximately $85.1 million through the year ended December 31, 2021.

Other Third Party Contracts

Under the Company's agreement with IQVIA, formerly known as Quintiles IMS, to provide contract research organization services for the $PRO_2TECT$ and $INNO_2VATE$ programs, the total remaining contract costs as of December 31, 2018 were approximately $106.3 million. The estimated period of substantive performance for the committed work with IQVIA is through the end of 2020. The Company also contracts with various other organizations to conduct research and development activities with remaining contract costs to the Company of approximately $102.8 million at December 31, 2018. The scope of the services under these research and development contracts can be modified and the contracts cancelled by the Company upon written notice. In some instances, the contracts may be cancelled by the third party upon written notice.

17. Net Loss per Share

The shares in the table below were excluded from the calculation of diluted net loss per share, prior to the use of the treasury stock method, due to their anti-dilutive effect:

| | Year ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Warrants | 509,611 | 509,611 | — |
| Outstanding stock options | 8,346,888 | 3,660,014 | 3,148,006 |
| Unvested restricted stock | — | — | 92,972 |
| Unvested restricted stock units | 962,316 | 728,738 | 431,688 |
| Total | 9,818,815 | 4,898,363 | 3,672,666 |

18. Quarterly Results (unaudited)

| | Three Months Ended | | | |
|---|---|---|---|---|
| | March 31, 2018 | June 30, 2018 | September 30, 2018 | December 31, 2018 |
| | (in thousands, except per share data) | | | |
| | (unaudited) | | | |
| Product revenue, net | $— | $— | $— | $6,824 |
| License, collaboration and other revenue | $45,930 | $48,793 | $53,169 | $53,026 |
| Cost of goods sold | $— | $— | $— | $7,768 |
| Operating expenses | $70,428 | $84,455 | $81,012 | $142,240 |
| Loss from operations | $(24,498) | $(35,662) | $(27,843) | $(90,158) |
| Other income, net | $1,080 | $1,593 | $1,796 | $1,766 |
| Benefit for income taxes | $— | $— | $— | $(28,338) |
| Net income (loss) | $(23,418) | $(34,069) | $(26,047) | $(60,054) |
| Net income (loss) per share: | | | | |
| basic and diluted | $(0.48) | $(0.60) | $(0.46) | $(0.87) |
| Weighted-average number of common shares: | | | | |
| basic and diluted | 48,613,565 | 56,890,295 | 57,027,598 | 69,404,187 |

| | Three Months Ended | | | |
|---|---|---|---|---|
| | March 31, 2017 | June 30, 2017 | September 30, 2017 | December 31, 2017 |
| | (in thousands, except per share data) | | | |
| | | (unaudited) | | (a) |
| Collaboration revenue | $20,865 | $28,520 | $41,283 | $90,559 |
| Total expenses | $65,837 | $50,656 | $65,459 | $75,949 |
| Loss from operations | $(44,972) | $(22,136) | $(24,176) | $14,610 |

| | | | | |
|---|---|---|---|---|
| Other income (expense), net | $429 | $618 | $1,042 | $914 |
| Net loss | $(44,543) | $(21,518) | $(23,134) | $15,524 |
| Net income (loss) per share: | | | | |
| basic | $(1.15) | $(0.53) | $(0.49) | $0.33 |
| diluted | $(1.15) | $(0.53) | $(0.49) | $0.31 |
| Weighted-average number of common shares: | | | | |
| basic | 38,759,221 | 40,819,957 | 46,938,618 | 47,353,166 |
| diluted | 38,759,221 | 40,819,957 | 46,938,618 | 49,719,548 |

(a) Revenue amount for the quarter ended December 31, 2017 has been revised to reflect the adoptions of ASC 606, with full retrospective application.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure
None.

Item 9A. Controls and Procedures
Management's Annual Report on Internal Control over Financial Reporting

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act). Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. 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 policy or procedures may deteriorate. Management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO. Based on the assessment, management has concluded that our internal control over financial reporting as of December 31, 2018 was effective to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with U.S. GAAP.

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

As of December 31, 2018, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. 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. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of December 31, 2018, our disclosure controls and procedures were effective at the reasonable assurance level.

Management has excluded from its assessment of and conclusion on the effectiveness of internal control over financial reporting the internal controls of Keryx, acquired on December 12, 2018, which is included in the consolidated financial statements of Akebia as of and for the year ended December 31, 2018 aggregating $126.3 million (including $70.2 million in inventory), or 13%, and $49.7 million, or 8%, of total and net assets, respectively, and $6.9 million, or 3%, and $3.8 million, or 2%, of revenues and pre-tax losses, respectively, for the year then ended.

Changes in Internal Control over Financial Reporting

There have been no changes in the Company's internal control over financial reporting during the fourth quarter of 2018, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Exchange Act, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information
Not applicable.

PART III

Item 10. Director, Executive Officers and Corporate Governance

The information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) Documents filed as part of this Annual Report on Form 10-K.

(1) Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations and Comprehensive Loss

Consolidated Statements of Stockholders' Equity (Deficit)

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Schedules

Schedules have been omitted as all required information has been disclosed in the financial statements and related footnotes.

(3) Exhibits

The Exhibits listed below are filed as part of this Annual Report on Form 10-K.

| Exhibit Number | Description of Exhibit |
|---|---|
| 2.1 | Agreement and Plan of Merger, dated as of June 28, 2018, by and among Akebia Therapeutics, Inc., Alpha Therapeutics Merger Sub, Inc., and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 2.1 to the Company's Current Report on Form 8-K, filed on June 28, 2018) ** |
| 2.2 | First Amendment to Agreement and Plan of Merger, dated as of October 1, 2018, by and among Akebia Therapeutics, Inc., Alpha Therapeutics Merger Sub, Inc. and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 2.1 to the Company's Current Report on Form 8-K, filed on October 1, 2018) |
| 3.1 | Ninth Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on March 28, 2014) |
| 3.2 | |

| | |
|---|---|
| | Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K, filed on March 28, 2014) |
| 4.1 | Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014) |
| 4.2 | Fourth Amended and Restated Investors' Rights Agreement, dated March 5, 2014 (incorporated by reference to Exhibit 4.4 to the Company's 10-K for the year ending December 31, 2014 and filed on March 4, 2015) |
| 4.3# | Common Stock Purchase Warrant between Akebia Therapeutics, Inc. and Janssen Pharmaceutica NV, dated February 9, 2017 (incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q, filed on May 9, 2017) |
| 4.4# | Investment Agreement between Akebia Therapeutics, Inc. and Vifor (International) Ltd., dated May 12, 2017 (incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q, filed on August 8, 2017) |
| 4.5 | Amendment No. 1 to Fourth Amended and Restated Investors' Rights Agreement, dated June 28, 2017 (incorporated by reference to Exhibit 4.5 to the Company's Annual Report on Form 10-K, filed on March 12, 2018) |

| Exhibit Number | Description of Exhibit |
|---|---|
| 10.1† | Form of Director and Officer Indemnification Agreement (incorporated by reference to Exhibit 10.1 to the Company's Annual Report on Form 10-K, filed on March 12, 2018) |
| 10.2 | Office Lease Agreement Between MA-Riverview/245 First Street, L.L.C. and Akebia Therapeutics, Inc., dated December 3, 2013 (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014) |
| 10.3 | First Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated December 15, 2014 (incorporated by reference to Exhibit 10.3 to the Company's 10-K for the year ending December 31, 2014 and filed on March 4, 2015) |
| 10.4 | Second Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated November 23, 2015 (incorporated by reference to Exhibit 10.4 to the Company's 10-K for the year ending December 31, 2015 and filed on March 14, 2016) |
| 10.5 | Third Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated July 25, 2016 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on November 9, 2016) |
| 10.6 | Fourth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc., dated May 1, 2017 (incorporated by reference to Exhibit 10.6 to the Company's 10-K for the year ending December 31, 2017, filed on March 12, 2018) |
| 10.7† | Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014) |
| 10.8† | Amendment No. 1 to Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014) |
| 10.9† | Executive Employment Agreement with John P. Butler, dated September 16, 2013 (incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014) |
| 10.10† | Executive Employment Agreement with Jason A. Amello, dated September 23, 2013 (incorporated by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014) |
| 10.11† | Form of Non-Statutory Stock Option Agreement for officers (incorporated by reference to Exhibit 10.24 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014) |
| 10.12† | Form of Non-Statutory Stock Option Agreement for non-employee directors (incorporated by reference to Exhibit 10.25 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014) |
| 10.13† | |

| | |
|---|---|
| | Amended and Restated Non-Employee Director Compensation Program, effective January 1, 2018 (incorporated by reference to Exhibit 10.13 to the Company's 10-K for the year ending December 31, 2017 and filed on March 12, 2018) |
| 10.14† | Form of Executive Severance Agreement for officers (incorporated by reference to Exhibit 10.27 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014) |
| 10.15† | 2014 Incentive Plan (incorporated by reference to exhibit 10.29 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014) |
| 10.16† | 2014 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.30 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014) |
| 10.17† | Cash Incentive Plan (incorporated by reference to Exhibit 10.31 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014) |
| 10.18† | Form of Officer Restricted Stock Unit Award Agreement under 2014 Incentive Plan (incorporated by reference to Exhibit 10.18 to the Company's Annual Report on Form 10-K, filed on March 12, 2018) |

| Exhibit Number | Description of Exhibit |
|---|---|
| 10.19† | Form of Officer Inducement Award Non-Statutory Stock Option Agreement (incorporated by reference to Exhibit 4.4 to the Company's Registration Statement on Form S-8 (333-222728), filed on January 26, 2018) |
| 10.20† | Form of Inducement Award Non-Statutory Stock Option Agreement for non-officers (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form S-8 (333-222728), filed on January 26, 2018) |
| 10.21# | Master Services Agreement, between Akebia Therapeutics, Inc., and Quintiles, Inc., dated as of June 8, 2015 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on August 11, 2015) |
| 10.22# | Collaboration Agreement between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation, dated December 11, 2015 (incorporated by reference to Exhibit 10.29 to the Company's 10-K for the year ending December 31, 2015 and filed on March 14, 2016) |
| 10.23# | Letter Agreement between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation, dated September 26, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on November 8, 2017) |
| 10.24# | Collaboration and License Agreement, between Akebia Therapeutics, Inc. and Otsuka Pharmaceutical Co. Ltd., dated December 18, 2016 (incorporated by reference to Exhibit 10.26 to the Company's 10-K for the year ending December 31, 2016 and filed on March 6, 2017) |
| 10.25# | Collaboration and License Agreement between Akebia Therapeutics, Inc. and Otsuka Pharmaceutical Co. Ltd., dated April 25, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on August 8, 2017) |
| 10.26# | Research and License Agreement between Akebia Therapeutics, Inc. and Janssen Pharmaceutica NV, dated February 9, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on May 9, 2017) |
| 10.27# | License Agreement between Akebia Therapeutics, Inc. and Vifor (International) Ltd., dated May 12, 2017 (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q, filed on August 8, 2017) |
| 10.28† | Offer Letter to Rita Jain, dated April 28, 2017 (incorporated by reference to Exhibit 10.28 to the Company's Annual Report on Form 10-K, filed on March 12, 2018) |
| 10.29*† | Form of Officer Restricted Stock Unit Award Agreement under 2014 Incentive Plan |
| 10.30 | [reserved] |
| 10.31*† | Amended and Restated Non-Employee Director Compensation Program, effective January 30, 2019 |
| 10.32† | Amendment No. 1 to the Akebia Therapeutics, Inc. 2014 Incentive Plan (incorporated by reference to Exhibit 4.4 to the Company's Registration Statement on Form S-8, filed on January 25, 2019) |

| | |
|---|---|
| 10.33 | Fifth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc. dated April 9, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on August 8, 2018) |
| 10.34 | Registration Rights Agreement, dated December 12, 2018, by and between Akebia Therapeutics, Inc. and Baupost Group Securities, L.L.C. (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, filed on December 13, 2018) |
| 10.35 | Notes Conversion Agreement, dated as of June 28, 2018, by and among Akebia Therapeutics, Inc., Keryx Biopharmaceuticals, Inc. and Baupost Group Securities, L.L.C. (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, filed on June 28, 2018) |
| 10.36# | Amended and Restated License Agreement by and between Panion & BF Biotech, Inc. and Keryx Biopharmaceuticals, Inc. dated March 17, 2008 (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q, filed on May 10, 2018) |

| Exhibit Number | Description of Exhibit |
|---|---|
| 10.37# | First Amendment to Amended and Restated License Agreement by and between Panion & BF Biotech, Inc. and Keryx Biopharmaceuticals, Inc. dated March 17, 2008 (incorporated by reference to Exhibit 10.16 to Keryx Biopharmaceuticals, Inc.'s Annual Report on Form 10-K, filed on March 31, 2009) |
| 10.38*! | Letter Agreement by and between Panion & BF Biotech, Inc., the Company and Keryx Biopharmaceuticals, Inc. dated October 24, 2018 |
| 10.39# | Amended and Restated Sub-License Agreement, dated June 8, 2009, as amended by the First Amendment thereto, dated June 12, 2013, by and between Keryx Biopharmaceuticals, Inc., Japan Tobacco, Inc. and Torii Pharmaceutical Co., Ltd (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q, filed on November 7, 2017) |
| 10.40# | Master Manufacturing Services Agreement by and between Keryx Biopharmaceuticals, Inc. and Patheon Manufacturing Services LLC and certain of its affiliates, dated September 27, 2016, and related Product Agreement dated September 27, 2016, and related Product Agreement dated October 12, 2016 (incorporated by reference to Exhibit 10.12 to Keryx Biopharmaceuticals, Inc.'s Annual Report on Form 10-K, filed on March 1, 2017) |
| 10.41# | Product Agreement, dated August 29, 2017, by and between Keryx Biopharmaceuticals, Inc. and Patheon Inc. (an affiliate of Patheon Manufacturing Services LLC) related to the Master Manufacturing Services Agreement by and between Keryx Biopharmaceuticals, Inc. and Patheon Manufacturing Services LLC and certain of its affiliates dated November 12, 2016 (incorporated by reference to Exhibit 10.2 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q, filed on November 7, 2017) |
| 10.42# | Product Manufacture and Supply and Facility Construction Agreement, dated December 11, 2017, by and between Keryx Biopharmaceuticals, Inc. and BioVectra Inc. (incorporated by reference to Exhibit 10.12 to Keryx Biopharmaceuticals, Inc.'s Annual Report on Form 10-K, filed on February 21, 2018) |
| 10.43# | Master Manufacturing Services and Supply Agreement, dated December 20, 2017, by and between Keryx Biopharmaceuticals, Inc. and Siegfried Evionnaz SA (incorporated by reference to Exhibit 10.13 to Keryx Biopharmaceuticals, Inc.'s Annual Report on Form 10-K, filed on February 21, 2018) |
| 10.44 | One Marina Park Drive Office Lease dated April 29, 2015, by and between Keryx Biopharmaceuticals, Inc. and Fallon Cornerstone One MPD LLC (incorporated by reference to Exhibit 10.29 to Keryx Biopharmaceuticals, Inc.'s Annual Report on Form 10-K, filed on March 1, 2017) |
| 10.45# | Amendment No. 1 to the Product Manufacture and Supply and Facility Construction Agreement, dated May 5, 2018, by and between Keryx Biopharmaceuticals, Inc. and BioVectra Inc. (incorporated by reference to Exhibit 10.6 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q, filed on August 9, 2018) |
| 10.46# | Loan and Security Agreement by and between Keryx Biopharmaceuticals, Inc. and Silicon Valley Bank, dated July 18, 2018 (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Current Report on Form 8-K, filed on July 20, 2018) |
| 10.47† | Keryx Biopharmaceuticals, Inc. 1999 Stock Option Plan (incorporated by reference to Exhibit 10.2 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q, filed on March 21, 2003) |

| | |
|---|---|
| 10.48† | Keryx Biopharmaceuticals, Inc. 2004 Long-Term Incentive Plan (incorporated by reference to Keryx Biopharmaceuticals, Inc.'s Definitive Proxy Statement on Schedule 14A, filed on April 29, 2004) |
| 10.49† | Amendment to the Keryx Biopharmaceuticals, Inc. 2004 Long-Term Incentive Plan dated April 11, 2006 (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q, filed on August 9, 2006) |
| 10.50† | Keryx Biopharmaceuticals, Inc. 2007 Incentive Plan, (incorporated by reference to Annex D to Keryx Biopharmaceuticals, Inc.'s Definitive Proxy Statement on Schedule 14A, filed on April 30, 2007) |
| 10.51† | Keryx Biopharmaceuticals, Inc. Amended and Restated 2013 Incentive Plan (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Current Report on Form 8-K, filed on May 27, 2016) |

| Exhibit Number | Description of Exhibit |
|---|---|
| 10.52† | Keryx Biopharmaceuticals, Inc. 2018 Equity Incentive Plan (incorporated by reference to Exhibit 99.1 to Keryx Biopharmaceuticals, Inc.'s Registration Statement on Form S-8, filed on June 29, 2018) |
| 10.53† | Form of Indemnification Agreement between Keryx Biopharmaceuticals, Inc. and its directors and officers (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q, filed on November m 2016) |
| 10.54† | Employment Agreement by and between Keryx Biopharmaceuticals, Inc. and Jodie Morrison dated May 10, 2018 (incorporated by reference to Exhibit 10.5 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q, filed on May 10, 2018) |
| 10.55† | Amendment to Employment Agreement by and between Keryx Biopharmaceuticals, Inc. and Jodie Morrison dated as of October 31, 2018 (incorporated by reference to Exhibit 10.2 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q, filed on November 8, 2018) |
| 10.56*† | Form of Employee Agreement (Confidentiality, Non-Competition, Non-Solicitation and Development Agreement) applicable to officers |
| 10.57† | Keryx Biopharmaceuticals, Inc. Fourth Amended and Restated Directors Equity Compensation Plan (incorporated by reference to Exhibit 10.2 to Keryx Biopharmaceuticals, Inc.'s Current Report on Form 8-K, filed on May 27, 2016) |
| 10.58† | Keryx Biopharmaceuticals, Inc. Third Amended and Restated Directors Equity Compensation Plan (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q for the quarter ended June 30, 2014, filed on August 7, 2014) |
| 10.59*† | Keryx Biopharmaceuticals, Inc. Director Non-Statutory Stock Option Award Terms and Conditions under the Third Amended and Restated Directors Equity Compensation Plan |
| 10.60*! | Exclusive Distribution Agreement between Keryx Biopharmaceuticals, Inc. and Cardinal Health 105, Inc., dated October 16, 2014 and Amendment to Exclusive Distribution Agreement between Keryx Biopharmaceuticals, Inc. and Cardinal Health 105, Inc., dated April 14, 2015 |
| 10.61*! | Manufacture and Supply Agreement between Keryx Biopharmaceuticals, Inc. and BioVectra Inc., dated May 26, 2017 and Amendment to Manufacture and Supply Agreement between Keryx Biopharmaceuticals, Inc. and BioVectra Inc., dated December 11, 2017 |
| 10.62 | Form of Controlled Equity Offering$^{SM}$ Sales Agreement, by and between Akebia Therapeutics, Inc. and Cantor Fitzgerald & Co. (incorporated by reference to Exhibit 1.1 to the Company's Registration Statement on Form S-3, filed on May 5, 2016) |
| 21.1* | List of Subsidiaries |
| 23.1* | Consent of Ernst & Young LLP |

| | |
|---|---|
| 23.2* | Consent of UHY LLP |
| 31.1* | Certification of Principal Executive Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended |
| 31.2* | Certification of Principal Financial Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended |
| 32.1* | Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. 1350 |
| 99.1* | Akebia Therapeutics, Inc. and Keryx Biopharmaceuticals, Inc. Unaudited Pro Forma Condensed Combined Financial Statements |
| 99.2* | Historical Consolidated Financial Statements of Keryx Biopharmaceuticals, Inc. as of, and for the years ended December 31, 2017, 2016, and 2015 and the six months ended, June 30, 2018 |
| 101.INS* | XBRL Instance Document |
| 101.SCH* | XBRL Taxonomy Extension Schema Document |

| Exhibit Number | Description of Exhibit |
|---|---|
| 101.CAL* | XBRL Taxonomy Extension Calculation Linkbase Document |
| 101.DEF* | XBRL Taxonomy Extension Definition Linkbase Document |
| 101.LAB* | XBRL Taxonomy Extension Labels Linkbase Document |
| 101.PRE* | XBRL Taxonomy Extension Presentation Linkbase Document |

* Filed, or submitted electronically, herewith
† Indicates management contract or compensatory plan
# Indicates portions of the exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment
! Confidential treatment pending as to certain portions, which portions are omitted and filed separately with the Commission
** The schedules to the Agreement and Plan of Merger have been omitted pursuant to Item 601(b)(2) of Regulation S-K. The Company will furnish copies of such schedules to the Securities and Exchange Commission upon request by the Commission

Item 16. Form 10-K Summary

None.

SIGNATURES

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.

AKEBIA THERAPEUTICS, INC.

Date: March 26, 2019

By: /s/ John P. Butler
John P. Butler
Chief Executive Officer and President (Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this report was signed by the following persons on behalf of the registrant and in the capacities and on the date indicated.

Date: March 26, 2019

By: /s/ John P. Butler
John P. Butler
Director, Chief Executive Officer and President (Principal Executive Officer)

Date: March 26, 2019

By: /s/ Jason A. Amello
Jason A. Amello
Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)

Date: March 26, 2019

By: /s/ Adrian Adams
Adrian Adams
Chairman

Date: March 26, 2019

By: /s/ Scott A. Canute
Scott A. Canute
Director

Date: March 26, 2019

By: /s/ Mark J. Enyedy
Mark J. Enyedy
Director

Date: March 26, 2019

By: /s/ Steven C. Gilman
Steven C. Gilman
Director

By: /s/ Maxine Gowen

| | | |
|---|---|---|
| Date: March 26, 2019 | | Maxine Gowen<br>Director |
| Date: March 26, 2019 | By: | /s/ Michael T. Heffernan<br>Michael T. Heffernan<br>Director |
| Date: March 26, 2019 | By: | /s/ Jodie P. Morrison<br>Jodie P. Morrison<br>Director |
| Date: March 26, 2019 | By: | /s/ Michael Rogers<br>Michael Rogers<br>Director |
| Date: March 26, 2019 | By: | /s/ Cynthia Smith<br>Cynthia Smith<br>Director |