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

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the quarterly period ended March 31, 2023

OR

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

Commission File Number 001-36352

AKEBIA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

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

Registrant's telephone number, including area code: (617) 871-2098
n/a
(Former name, former address and former fiscal year, if changed since last report)

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

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.00001 per share	**AKBA**	**The Nasdaq Capital Market**

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

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

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

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

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

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

Indicate the number of shares outstanding of each of the issuer's classes of common stock, as of the latest practicable date.

Outstanding at April 30, 2023
185,928,121

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q 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. All statements contained in this Quarterly Report on Form 10-Q other than statements of historical fact are forward-looking statements. These forward-looking statements may be accompanied by words such as "anticipate," "believe," "build," "can," "contemplate," "continue," "could," "should," "designed," "estimate," "project," "expect," "forecast," "future," "goal," "intend," "likely," "may," "plan," "possible," "potential," "predict," "strategy," "seek," "target," "will," "would," and other words and terms of similar meaning, but the absence of these words does not necessarily mean that a statement is not forward-looking. These forward-looking statements include, but are not limited to, statements about:

- the potential therapeutic benefits, safety profile, and effectiveness of vadadustat;
- our expectations with respect to the development of vadadustat, if any, following our receipt of a complete response letter to our new drug application for vadadustat for the treatment of anemia due to chronic kidney disease in adult patients, including the timing of a potential response to the Formal Dispute Resolution Request from the U.S. Food and Drug Administration;
- that delivering value broadly to the kidney community, as well as others who may benefit from our medicines, will result in delivering value for stockholders;
- our pipeline and portfolio, including its potential, and our related research and development activities;
- the timing of or likelihood of regulatory filings and approvals, including with respect to labeling or other restrictions, the potential approval of vadadustat and our outlook related thereto, and potential indications for vadadustat;
- the timing, investment and associated activities involved in continued commercialization of Auryxia® (ferric citrate), its growth opportunities and our ability to execute thereon;
- the potential indications, demand and market opportunity, potential and acceptance of Auryxia and vadadustat, if approved, including the size of eligible patient populations;
- the potential therapeutic applications of the hypoxia inducible factor pathway;
- 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 capital requirements, need for additional capital, financing our future cash needs, costs, expenses, revenues, capital resources, cash flows, financial performance, profitability, tax obligations, liquidity, growth, contractual obligations, the period of time our cash resources will fund our current operating plan, estimates with respect to our ability to operate as a going concern, our internal control over financial reporting and disclosure controls and procedures, and any future deficiencies or material weaknesses in our internal controls and procedures;
- the direct or indirect impacts of the COVID-19 pandemic on our business, operations and the markets and communities in which we and our partners, collaborators, vendors, and customers operate;
- our manufacturing, supply and quality matters and any recalls, write-downs, impairments or other related consequences or potential consequences;
- estimates, beliefs and judgments related to the valuation of intangible assets, goodwill, debt and other assets and liabilities, including our impairment analysis and our methodology and assumptions regarding fair value measurements;
- 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, supply, commercialization, launch, marketing and sale of Auryxia and vadadustat, if approved, and the associated timing thereof;
- our plans with respect to commercializing and identifying a partner for Vafseo in Europe;
- the designs of our studies, and the type of information and data expected from our studies and the expected benefits thereof;
- 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 and vadadustat, if approved;

- the timing of initiation of our clinical trials and plans to conduct preclinical studies and clinical trials 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, patent infringement suits that we have filed or may file, or other actions that we may take against companies, and the timing and resolution thereof;
- expected ongoing reliance on third parties, including with respect to the development, manufacturing, supply and commercialization of Auryxia and vadadustat, if approved;
- 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;
- management of personnel, including our management team, and our employees, including employee compensation, employee relations, and our ability to attract, train 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;
- our workforce reductions, future charges expected to be incurred in connection therewith and estimated reductions in net cash required for operating activities in connection therewith; and
- the timing, outcome and impact of current and any future legal proceedings.

Any or all of these forward-looking statements in this Quarterly Report on Form 10-Q may turn out to be inaccurate. These forward-looking statements involve risks and uncertainties, including those that are discussed below under the heading "Risk Factor Summary", and the risk factors identified further in Part II, Item 1A. "Risk Factors" included in this Quarterly Report on Form 10-Q and elsewhere in this Quarterly Report on Form 10-Q, 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 Quarterly Report on Form 10-Q. 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 Quarterly Report on Form 10-Q 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 Quarterly Report on Form 10-Q, 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 Biopharmaceuticals, Inc.

RISK FACTORS SUMMARY

Investing in our common stock involves numerous risks, including the risks summarized below and described in further detail in "Part II, Item 1A. Risk Factors" of this Quarterly Report on Form 10-Q, any one of which could materially adversely affect our business, financial condition, results of operations, and prospects. These risks include, but are not limited to, the following:

- 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.
- We will require substantial additional financing to achieve our goals. A failure to obtain this necessary capital when needed, or on acceptable terms, could force us to delay, limit, reduce or terminate our product development or commercialization efforts.
- 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.
- If we fail to regain compliance with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.
- We may not be successful in our efforts to identify, acquire, in-license, discover, develop and commercialize additional products or product candidates or our decisions to prioritize the development of certain product candidates over others may not be successful, which could impair our ability to grow.
- 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.
- Our business has been and may continue to be, directly or indirectly, adversely affected by the COVID-19 pandemic.
- Our obligations in connection with the loan agreement with Pharmakon and requirements and restrictions in the loan agreement could adversely affect our financial condition and restrict our operations.
- Our Royalty Interest Acquisition Agreement with HealthCare Royalty Partners IV, L.P. contains various covenants and other provisions, which, if violated, could materially adversely affect our financial condition.
- Our business is substantially dependent on the commercial success of Auryxia. If we are unable to continue to successfully commercialize Auryxia, our results or operations and financial condition will be materially harmed.
- If we are unable to maintain or expand, or, if vadadustat is approved, initiate, sales and marketing capabilities or enter into additional agreements with third parties, we may not be successful in commercializing Auryxia, vadadustat, if approved, or any other product candidates that may be approved.
- Our, or our partners', failure to obtain or maintain adequate coverage, pricing and reimbursement for Auryxia, vadadustat, if approved, or any other future approved products, could have a material adverse effect on our or our collaboration partners' ability to sell such approved products profitably and otherwise have a material adverse impact on our business.
- We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully than, we do.
- The commercialization of Riona™ and Vafseo™ in Japan, Vafseo™ in Europe and our current and potential 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.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and, if approved, commercialization of vadadustat and any other product candidates.
- We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.
- Conducting clinical trials outside of the United States, as we have done historically and as we may decide to do in the future, presents additional risks and complexities and, if we decide to conduct a clinical trial outside of the United States in the future, we may not complete such trials successfully, in a timely manner, or at all, which could affect our ability to obtain regulatory approvals.
- Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, may cause undesirable side effects or have other properties that may delay or prevent marketing approval or limit their commercial potential.
- We may not be able to obtain marketing approval for, or successfully commercialize, vadadustat or any other product candidate, or we may experience significant delays in doing so, any of which would 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, including withdrawal of marketing approval, if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, or product candidates, when and if any of them is approved.
- We are subject to a complex regulatory scheme that requires significant resources to ensure compliance and our failure to comply with applicable laws could subject us to government scrutiny or enforcement, potentially resulting in costly investigations, fines, penalties or sanctions, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

- We will incur significant liability if it is determined that we are promoting any "off-label" use of Auryxia or any other product we may develop, in-license or acquire or if it is determined that any of our activities violates the federal Anti-Kickback Statute.
- Disruptions in the FDA, regulatory authorities outside the U.S. and other government agencies caused by global health concerns or funding shortages could prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.
- Compliance with 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.
- Legislative and regulatory healthcare reform 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.
- We depend on collaborations with third parties for the development and commercialization of Auryxia, Riona, Vafseo and vadadustat and if these 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, Riona, Vafseo and vadadustat, and our business could be materially harmed.
- We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans.
- We rely upon third parties to conduct all aspects of our product manufacturing, and in many instances only have a single supplier, and the loss of these manufacturers, their failure to supply us on a timely basis, or at all, or their failure to successfully carry out their contractual duties or comply with regulatory requirements, cGMP requirements, or guidance could cause delays in or disruptions to our supply chain and substantially harm our business.
- We rely upon third parties to conduct our clinical trials and certain of our preclinical studies. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain or maintain marketing approval for Auryxia, vadadustat or any of our product candidates, and our business could be substantially harmed.
- 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.
- 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.
- We may not be able to protect our intellectual property rights throughout the world.
- The intellectual property that we own or have licensed and related non-patent exclusivity relating to our current and future products is, and may be, limited, which could adversely affect our ability to compete in the market and adversely affect the value of Auryxia.
- The market entry of one or more generic competitors or any third party's attempt to challenge our intellectual property rights will likely limit Auryxia sales and have an adverse impact on our business and results of operation.
- Litigation and administrative proceedings, including third party claims of intellectual property infringement and opposition/invalidation proceedings against third party patents, may be costly and time consuming and may delay or harm our drug discovery, development and commercialization efforts.
- We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.
- If we fail to attract, retain and motivate senior management and qualified personnel, we may be unable to successfully develop, obtain and/or maintain marketing approval of and commercialize vadadustat or commercialize Auryxia.
- Our cost savings plan and the associated workforce reductions implemented in April, May and November 2022 may not result in anticipated savings, could result in total costs and expenses that are greater than expected and could disrupt our business.
- We may encounter difficulties in managing our growth, including with respect to our employee base, and managing our operations successfully.
- We are currently subject to legal proceedings that could result in substantial costs and divert management's attention, and we could be subject to additional legal proceedings.
- Our stock price has been and may continue to be volatile, which could result in substantial losses for holders or future purchasers of our common stock and lawsuits against us and our officers and directors.

Akebia Therapeutics, Inc.

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PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

AKEBIA THERAPEUTICS, INC.

Condensed Consolidated Balance Sheets
(Unaudited)
(in thousands, except share and per share data)

	March 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 56,953	$ 90,466
Inventory	20,604	21,762
Accounts receivable, net	17,781	39,180
Prepaid expenses and other current assets	25,381	33,541
Total current assets	120,719	184,949
Property and equipment, net	4,816	5,214
Operating lease assets	27,958	29,158
Goodwill	55,053	55,053
Other intangible assets, net	63,074	72,084
Other assets	5,238	5,372
Total assets	$ 276,858	$ 351,830
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 12,577	$ 18,021
Accrued expenses and other current liabilities	46,367	70,997
Short-term deferred revenue	—	3,738
Current portion of long-term debt	24,000	32,000
Total current liabilities	82,944	124,756
Deferred revenue, net of current portion	43,296	43,296
Operating lease liabilities, net of current portion	27,418	28,961
Derivative liability	760	760
Long-term debt, net	26,296	34,078
Liability related to sale of future royalties	57,059	57,484
Refund liability to customer	40,794	40,992
Other non-current liabilities	12,643	12,161
Total liabilities	291,210	342,488
Commitments and contingencies (Note 12)		
Stockholders' (deficit) equity:		
Preferred stock $0.00001 par value, 25,000,000 shares authorized; 0 shares issued and outstanding at March 31, 2023 and December 31, 2022	—	—
Common stock $0.00001 par value; 350,000,000 shares authorized at March 31, 2023 and December 31, 2022; 185,835,946 and 184,135,714 shares issued and outstanding at March 31, 2023 and December 31, 2022, respectively	2	2
Additional paid-in capital	1,564,770	1,562,247
Accumulated other comprehensive gain	6	6
Accumulated deficit	(1,579,130)	(1,552,913)
Total stockholders' (deficit) equity	(14,352)	9,342
Total liabilities and stockholders' (deficit) equity	$ 276,858	$ 351,830

See accompanying notes to unaudited condensed consolidated financial statements.

AKEBIA THERAPEUTICS, INC.

Condensed Consolidated Statements of Operations and Comprehensive Loss
(Unaudited)
(in thousands, except share and per share data)

	Three Months Ended March 31,	
	2023	**2022**
Revenues:		
Product revenue, net	$ 34,828	$ 41,448
License, collaboration and other revenue	5,299	20,251
Total revenues	40,127	61,699
Cost of goods sold:		
Product	10,473	22,333
Amortization of intangibles	9,011	9,011
Total cost of goods sold	19,484	31,344
Operating expenses:		
Research and development	19,686	43,833
Selling, general and administrative	25,221	44,327
License expense	568	688
Restructuring	106	—
Total operating expenses	45,581	88,848
Operating loss	(24,938)	(58,493)
Other income (expense):		
Interest expense	(1,561)	(5,062)
Other income	282	1,134
Net loss	$ (26,217)	$ (62,421)
Net loss per share - basic and diluted	$ (0.14)	$ (0.35)
Weighted-average number of common shares - basic and diluted	184,768,983	179,599,045
Comprehensive loss:		
Net loss	$ (26,217)	$ (62,421)
Total comprehensive loss	$ (26,217)	$ (62,421)

See accompanying notes to unaudited condensed consolidated financial statements.

AKEBIA THERAPEUTICS, INC.

Condensed Consolidated Statements of Stockholders' (Deficit) Equity
(Unaudited)
(in thousands, except share data)

	Common Stock					
	Number of Shares	$0.00001 Par Value	Additional Paid-In Capital	Unrealized Gain/(Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance at December 31, 2021	177,000,963	$ 1	$ 1,536,800	$ 6	$ (1,460,351)	$ 76,456
Issuance of common stock, net of issuance costs	4,404,600	1	7,177	—	—	7,178
Proceeds from sale of stock under employee stock purchase plan	191,146	—	367	—	—	367
Stock-based compensation expense	—	—	4,536	—	—	4,536
Restricted stock unit vesting	1,789,326	—	—	—	—	—
Net loss	—	—	—	—	(62,421)	(62,421)
Balance at March 31, 2022	183,386,035	$ 2	$ 1,548,880	$ 6	$ (1,522,772)	$ 26,116
Balance at December 31, 2022	184,135,714	$ 2	$ 1,562,247	$ 6	$ (1,552,913)	$ 9,342
Proceeds from sale of stock under employee stock purchase plan	103,500	—	34	—	—	34
Stock-based compensation expense	—	—	2,489	—	—	2,489
Restricted stock unit vesting	1,596,732	—	—	—	—	—
Net loss	—	—	—	—	(26,217)	(26,217)
Balance at March 31, 2023	185,835,946	$ 2	$ 1,564,770	$ 6	$ (1,579,130)	$ (14,352)

See accompanying notes to unaudited condensed consolidated financial statements

AKEBIA THERAPEUTICS, INC.

Condensed Consolidated Statements of Cash Flows
(Unaudited)
(in thousands)

	Three Months Ended	
	March 31, 2023	**March 31, 2022**
Operating activities:		
Net loss	$ (26,217)	$ (62,421)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	398	417
Amortization of intangibles	9,011	9,011
Non-cash interest expense related to sale of future royalties	—	2,345
Non-cash royalty revenue related to sale of future royalties	(425)	(329)
Non-cash R&D expense	782	—
Non-cash interest expense	502	246
Non-cash operating lease expense	(578)	(557)
Write-down of inventory	335	5,344
Change in excess inventory purchase commitments	—	(773)
Stock-based compensation	2,489	4,536
Change in fair value of derivative liability	—	(710)
Changes in operating assets and liabilities:		
Accounts receivable	21,399	(13,707)
Inventory	7,347	(5,247)
Prepaid expenses and other current assets	7,378	9,019
Other long-term assets	(2,812)	3,297
Accounts payable	(9,013)	(7,358)
Accrued expense	(25,047)	4,426
Operating lease liabilities	651	616
Deferred revenue	(3,738)	33,416
Other non-current liabilities	—	(3,191)
Net cash used in operating activities	(17,538)	(21,620)
Investing activities:		
Purchase of equipment	—	(114)
Net cash used in investing activities	—	(114)
Financing activities:		
Proceeds from refund liabilities to customers	—	40,000
Proceeds from the issuance of common stock, net of issuance costs	—	7,178
Proceeds from the sale of stock under employee stock purchase plan	34	367
Payments on debt	(16,000)	—
Net cash (used in) provided by financing activities	(15,966)	47,545
(Decrease) increase in cash, cash equivalents, and restricted cash	(33,504)	25,811
Cash, cash equivalents, and restricted cash at beginning of the period	93,169	151,839
Cash, cash equivalents, and restricted cash at end of the period	$ 59,665	$ 177,650

See accompanying notes to unaudited condensed 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 fully integrated biopharmaceutical company with the purpose of bettering the lives of people impacted by kidney disease. The Company has one commercial product, Auryxia® (ferric citrate), which is approved by the U.S. 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 IDA in adult patients for the improvement of hyperphosphatemia in such patients with DD-CKD and NDD-CKD under the trade name Riona (ferric citrate hydrate).

Vadadustat, the Company's lead investigational product candidate, is an investigational oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor designed to mimic the physiologic effect of altitude on oxygen availability. On March 29, 2022, the Company received a complete response letter, or CRL, from the FDA. The CRL provided that the FDA had completed its review of the Company's new drug application, or NDA, for vadadustat for the treatment of anemia due to CKD in adult patients and had determined that it could not approve the NDA in its present form. In October 2022, the Company submitted a Formal Dispute Resolution Request, or FDRR, with the FDA. The FDRR focused on the favorable balance between the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult DD-CKD patients in light of safety concerns expressed by the FDA in the CRL for dialysis patients related to the rate of adjudicated thromboembolic events driven by vascular access thrombosis for vadadustat compared to the active comparator and the risk of drug-induced liver injury. In February 2023, the Company received a second interim response from the FDA to the FDRR. In March 2023, the Company had a productive meeting with the FDA, who indicated that it was continuing internal consultation with experts to complete the review and render a decision. FDA has indicated that it has completed internal discussions, and the Company expects a response to the FDRR within the next thirty days. In October 2021, the Company's former collaboration partner, Otsuka Pharmaceutical Co. Ltd., or Otsuka, submitted a Marketing Authorization Application, or MAA, for vadadustat for the treatment of anemia due to CKD in adult patients with DD-CKD and NDD-CKD to the European Medicines Agency, or EMA. In connection with the Termination and Settlement Agreement with Otsuka dated June 30, 2022, or the Termination Agreement, Otsuka transferred the MAA for vadadustat with the EMA to the Company. In April 2023, the European Commission, or EC, approved the marketing authorization of vadadustat under the trade name Vafseo™ for the treatment of symptomatic anemia associated with CKD in adults on chronic maintenance dialysis. Vadadustat is approved in Japan as a treatment for anemia due to CKD in both DD-CKD and NDD-CKD patients under the trade name Vafseo™, and marketed and sold in Japan by Mitsubishi Tanabe Pharma Corporation, or MTPC. Vadadustat is also approved in Korea as a treatment for anemia due to CKD in DD-CKD patients.

In addition, the Company continues to explore additional development opportunities to expand its pipeline and portfolio of novel therapeutics.

Since inception, the Company has devoted most of its resources to research and development, including its preclinical and clinical development activities, commercializing Auryxia, and providing general and administrative support for these operations. The Company began recording revenue from the U.S. sales of Auryxia and revenue from sublicensing rights to Auryxia in Japan from the Company's Japanese partners, Japan Tobacco, Inc. and its subsidiary Torii Pharmaceutical Co., Ltd., collectively JT and Torii, in December 2018. Additionally, following regulatory approval of vadadustat in Japan, the Company began recognizing royalty revenues from MTPC from the sale of Vafseo in August 2020. In February 2021, the Company entered into a royalty interest acquisition agreement with HealthCare Royalty Partners IV, L.P., or HCR, or the Royalty Agreement, whereby the Company sold its right to receive royalties and sales milestones under its Collaboration Agreement with MTPC, or the MTPC Agreement, subject to certain caps and other terms and conditions (see Note 5 for additional information). The Company has not generated a profit to date, and may never generate profits, from product sales. Vadadustat and the Company's other potential 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 vadadustat and its other potential product candidates. If the Company does not successfully commercialize Auryxia, vadadustat, if approved, or any other potential product candidate, it may be unable to achieve profitability.

The Company's management completed its going concern assessment in accordance with Accounting Standards Codification, or ASC, 205-40, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, or ASC 205-40. As of March 31, 2023, the Company had cash and cash equivalents of approximately $57.0 million. Based on its current operating plan, 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 this Quarterly Report on Form 10-Q. If the Company's operating performance deteriorates significantly from the levels expected in the Company's operating plan, it could have an effect on the Company's liquidity and its ability to continue as a going concern in the future. The Company expects to finance future cash needs through product revenue, potential strategic transactions, public or private equity or debt transactions, operating expense management, or a combination of these approaches. Assuming the Company is successful in executing its operating plan, the Company will require additional funding to fund its strategic growth beyond Auryxia or to pursue later stage development and commercial activities for its product candidates and any additional product or product candidates, including those that may be in-licensed or acquired. There can be no assurance that the current operating plan will be achieved in the time frame anticipated by the Company, or that its cash resources will fund its 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.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the U.S., or GAAP, for interim financial reporting and as required by Regulation S-X, Rule 10-01. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the ASC and Accounting Standards Update, or ASU, of the Financial Accounting Standards Board, or FASB.

In the opinion of management, all adjustments, consisting of normal recurring accruals and revisions of estimates, considered necessary for a fair presentation of the unaudited condensed consolidated financial statements have been included. Interim results for the three months ended March 31, 2023 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2023 or any other future period.

The accompanying unaudited condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. Management has determined that the Company operates in one segment, which is the business of developing and commercializing novel therapeutics for people with kidney disease. The information included in this Quarterly Report on Form 10-Q should be read in conjunction with the Company's consolidated financial statements and the accompanying notes included in the Company's Annual Report on Form 10-K for the year ended December 31, 2022 filed with the U.S. Securities and Exchange Commission on March 10, 2023, or the 2022 Annual Report on Form 10-K.

The significant accounting policies used in preparation of these unaudited condensed consolidated financial statements for the three months ended March 31, 2023 are consistent with those discussed in Note 2 to the consolidated financial statements in the Company's 2022 Annual Report on Form 10-K and are updated below as necessary.

Use of Estimates

The preparation of financial statements in conformity with 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, operating lease assets and liabilities, derivative liabilities, refund liabilities to customers, other non-current liabilities, stock-based compensation expense, product and collaboration revenues including various rebates and reserves related to product sales, non-cash interest expense on the liability related to sale of future royalties, inventories, income taxes, intangible assets and goodwill.

Although the Company regularly assesses these estimates, actual results could differ materially from these estimates. Changes in estimates are recorded in the period they become known. The Company bases its estimates on historical experience and various other assumptions that it believes to be reasonable under the circumstances.

3. Product Revenue and Reserves for Variable Consideration

To date, the Company's only source of product revenue has been from the U.S. sales of Auryxia. Total net product revenue was $34.8 million and $41.4 million for the three months ended March 31, 2023 and 2022, respectively. The following table summarizes activity in each of the product revenue allowance and reserve categories for the three months ended March 31, 2023 and 2022 (in thousands):

	Chargebacks and Discounts	Rebates, Fees and other Deductions	Returns	Total
Balance at December 31, 2022	$ 1,476	$ 28,990	$ 887	$ 31,353
Current provisions related to sales in current year	1,608	16,965	1,578	20,151
Adjustments related to prior year sales	(482)	(1,266)	—	(1,748)
Credits/payments made	(1,997)	(22,321)	(1,631)	(25,949)
Balance at March 31, 2023	$ 605	$ 22,368	$ 834	$ 23,807
Balance at December 31, 2021	$ 1,278	$ 26,625	$ 475	$ 28,378
Current provisions related to sales in current year	2,711	21,324	1,359	25,394
Adjustments related to prior year sales	(132)	779	—	647
Credits/payments made	(2,465)	(22,491)	(1,293)	(26,249)
Balance at March 31, 2022	$ 1,392	$ 26,237	$ 541	$ 28,170

Chargebacks, discounts and returns are recorded as a direct reduction of revenue on the unaudited condensed consolidated statement of operations with a corresponding reduction to accounts receivable on the unaudited condensed consolidated balance sheets. Rebates, distribution-related fees, and other sales-related deductions are recorded as a reduction in revenue on the unaudited condensed consolidated statement of operations with a corresponding increase to accrued liabilities or accounts payable on the unaudited condensed consolidated balance sheets.

Accounts receivable, net related to product sales was approximately $17.3 million and $36.2 million as of March 31, 2023 and December 31, 2022, respectively.

4. License, Collaboration and Other Significant Agreements

During the three months ended March 31, 2023 and 2022, the Company recognized the following revenues from its license, collaboration and other significant agreements and had the following deferred revenue balances as of March 31, 2023:

	Three Months Ended March 31,	
	2023	2022
License, Collaboration and Other Revenue:	(in thousands)	
MTPC Agreement	$ 4,162	$ 7,962
Otsuka U.S. Agreement	—	5,638
Otsuka International Agreement	—	5,503
Total Proportional Performance Revenue	$ 4,162	$ 19,103
JT and Torii	1,137	1,148
Total License, Collaboration and Other Revenue	$ 5,299	$ 20,251

	March 31, 2023		
	Short-Term	Long-Term	Total
Deferred Revenue:	(in thousands)		
CSL Vifor Agreement	$ —	$ 43,296	$ 43,296
Total	$ —	$ 43,296	$ 43,296

The following table presents changes in the Company's contract assets and liabilities during the three months ended March 31, 2023 and 2022 (in thousands):

Three Months Ended March 31, 2023	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Contract assets:				
Accounts receivable(1)	$ 1,901	$ 417	$ (1,901)	$ 417
Prepaid expenses and other current assets	$ 781	$ —	$ (781)	$ —
Contract liabilities:				
Deferred revenue	$ 47,034	$ —	$ (3,738)	$ 43,296
Three Months Ended March 31, 2022				
Contract assets:				
Accounts receivable(1)	$ 19,094	$ 19,542	$ (14,320)	$ 24,316
Prepaid expenses and other current assets	$ 4,309	$ —	$ (339)	$ 3,970
Contract liabilities:				
Deferred revenue	$ 42,380	$ 60,514	$ (27,098)	$ 75,796
Accounts payable	$ 3,171	$ —	$ (2,852)	$ 319

(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 as of March 31, 2023 and 2022 and December 31, 2022 and 2021. Also excludes accounts receivable related to amounts due to the Company from product sales which are included in the accompanying unaudited condensed consolidated balance sheet as of March 31, 2023 and 2022.

During the three months ended March 31, 2023 and 2022, 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):

	Three Months Ended March 31,	
Revenue Recognized in the Period:	**2023**	**2022**
Amounts included in deferred revenue at the beginning of the period	$ 3,738	$ 6,602
Performance obligations satisfied in previous periods	$ —	$ —

Mitsubishi Tanabe Pharma Corporation Collaboration Agreement

Summary of Agreement

On December 11, 2015, the Company and MTPC entered into the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to vadadustat in Japan and certain other Asian countries, collectively, the MTPC Territory, which was amended effective as of December 2, 2022. In addition, the Company supplies vadadustat to MTPC for both clinical and commercial use in the MTPC Territory. In February 2021, the Company entered into the Royalty Agreement with HCR, whereby the Company sold its right to receive royalties and sales milestones under the MTPC Agreement, subject to certain caps and other terms and conditions (see Note 5 for additional information). A more detailed description of the MTPC Agreement and the Company's evaluation of this agreement under ASC 606 can be found in Note 4 of the Notes to the Consolidated Financial Statements in the 2022 Annual Report on Form 10-K.

The Company identified two performance obligations in connection with its material promises under the MTPC Agreement as follows: (i) *License, Research and Clinical Supply Performance Obligation* and (ii) *Rights to Future Know-How 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 is immaterial. As such, the Company did not develop a best estimate of standalone selling price for the License, Research and Clinical Supply Performance

Obligation and allocated the entire transaction price to this performance obligation. The deliverables associated with the License, Research and Clinical Supply Performance Obligation were satisfied as of June 30, 2018.

As of March 31, 2023, the transaction price was 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, (iv) $10.0 million in development milestones received, (v) $25.0 million in regulatory milestones received, comprised of $10.0 million relating to the NDA filing in Japan and $15.0 million relating to regulatory approval of vadadustat in Japan, and (vi) $3.4 million in royalties from net sales of Vafseo. As of March 31, 2023, all development milestones and $25.0 million in regulatory milestones have been achieved. No other regulatory milestones have been assessed as probable of being achieved and as a result have been fully constrained. The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. Revenue for the License, Research and Clinical Supply Performance Obligation for the MTPC Agreement is being recognized using a proportional performance method, for which all deliverables have been completed. During the three months ended March 31, 2023 and 2022, the Company recognized revenue from MTPC royalties totaling approximately $0.4 million and $0.3 million, respectively. As noted above, in February 2021, the Company entered into the Royalty Agreement, whereby the Company sold its right to receive these royalties and sales milestones under the MTPC Agreement, subject to certain caps and other terms and conditions (see Note 5 for additional information). The revenue is classified as license, collaboration and other revenue in the accompanying unaudited condensed consolidated statements of operations and comprehensive loss. As of March 31, 2023, the Company recorded $0.2 million in accounts receivable, no deferred revenue, and no contract assets. There were no asset or liability balances classified as long-term in the unaudited condensed consolidated balance sheet as of March 31, 2023.

Supply of Drug Product to MTPC

On July 15, 2020, the Company and its collaboration partner MTPC entered into a supply agreement, or the MTPC Supply Agreement. The MTPC Supply Agreement includes the terms and conditions under which the Company will supply vadadustat drug product to MTPC for commercial use in Japan and certain other Asian countries, as contemplated by the MTPC Agreement. A more detailed description of this supply agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the 2022 Annual Report on Form 10-K.

On December 16, 2022, the Company, MTPC, and Esteve Química, S.A., or Esteve, executed an Assignment of Supply Agreement, or the Assignment Agreement, pursuant to which the Supply Agreement between the Company and Esteve (see Note 12), or the Esteve Agreement, was assigned to MTPC. The Assignment Agreement transferred the rights and obligations of the Company under the Esteve Agreement to MTPC, including the obligations under certain purchase orders issued by the Company and accepted by Esteve. As such, the transferred purchase orders will continue to have a binding effect on MTPC to take delivery of the product from Esteve in accordance with the terms of the Esteve Agreement. The Company will have no further obligation to take delivery of, or pay for, product delivered by Esteve under the transferred purchase orders.

The Company recognized $3.7 million and $7.6 million in revenue under the MTPC Supply Agreement during the three months ended March 31, 2023 and 2022, respectively. As of March 31, 2023, the Company recorded no accounts receivable, no deferred revenue and no other current liabilities.

U.S. Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

On December 18, 2016, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement. The collaboration was focused on the development and commercialization of vadadustat in the United States. The Company was responsible for leading the development of vadadustat, for which it submitted an NDA to the FDA in March 2021, and for which it received the CRL in March 2022. On May 12, 2022, the Company received notice from Otsuka that Otsuka had elected to terminate the Otsuka U.S. Agreement and the April 25, 2017 collaboration and license agreement with Otsuka, or the Otsuka International Agreement. On June 30, 2022, the Company and Otsuka entered into the Termination Agreement, pursuant to which, among other things, the Company and Otsuka agreed to terminate the Otsuka U.S. Agreement and the Otsuka International Agreement as of June 30, 2022.

A more detailed description of this collaboration agreement and the Company's evaluation of this agreement under ASC 606 can be found in Note 4 of the Notes to the Consolidated Financial Statements in the 2022 Annual Report on Form 10-K.

During the three months ended March 31, 2022, the Company recognized collaboration revenue totaling $5.6 million with respect to the Otsuka U.S. Agreement.

International Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

On April 25, 2017, the Company entered into the Otsuka International Agreement. The collaboration was 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. As discussed above, the Otsuka International Agreement was terminated on June 30, 2022 pursuant to the Termination Agreement.

A more detailed description of this collaboration agreement and the Company's evaluation of this agreement under ASC 606 can be found in Note 4 of the Notes to the Consolidated Financial Statements in the 2022 Annual Report on Form 10-K.

During the three months ended March 31, 2022, the Company recognized collaboration revenue totaling approximately $5.5 million with respect to the Otsuka International Agreement.

Cyclerion Therapeutics License Agreement

On June 4, 2021, the Company entered into a License Agreement, the Cyclerion Agreement, with Cyclerion Therapeutics Inc., or Cyclerion, pursuant to which Cyclerion granted the Company an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate stimulator.

Under the terms of the Cyclerion Agreement, the Company made an upfront payment of $3.0 million in cash to Cyclerion, which was paid and recorded to research and development expense in June 2021. Substantially all of the fair value of the assets acquired in conjunction with the Cyclerion Agreement was concentrated in the acquired license. As a result, the Company accounted for this transaction as an asset acquisition under ASU No. 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business*. The upfront payment was charged to expense at acquisition, as it relates to a development stage compound with no alternative future use. In addition, Cyclerion is eligible to receive up to an aggregate of $222.0 million from the Company in specified development and regulatory milestone payments on a product-by-product basis. Cyclerion will also be eligible to receive specified commercial milestones as well as tiered royalties ranging from a low-single-digit- to mid-double-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. A more detailed description of this agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the 2022 Annual Report on Form 10-K.

CSL Vifor License Agreement

Summary of License Agreement

On May 12, 2017, the Company entered into a License Agreement, or the Vifor Agreement, with Vifor (International) Ltd. (now a part of CSL Limited), or CSL Vifor, pursuant to which the Company granted CSL Vifor an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, an affiliate of Fresenius Medical Care North America, or FMCNA, in the United States. On April 8, 2019, the Company and CSL Vifor entered into an Amended and Restated License Agreement, or the Vifor First Amended Agreement, which amended and restated in full the Vifor Agreement. On February 18, 2022, the Company and CSL Vifor entered into a Second Amended and Restated License Agreement, or the Vifor Second Amended Agreement, which amends and restates the Vifor First Amended Agreement.

Pursuant to the Vifor Second Amended Agreement, the Company granted CSL Vifor an exclusive license to sell vadadustat to FMCNA and its affiliates, including Fresenius Kidney Care Group LLC, to certain third party dialysis organizations approved by the Company, to independent dialysis organizations that are members of certain group purchasing organizations, and to certain non-retail specialty pharmacies, or collectively, the Supply Group, in the United States, or the Territory. Pursuant to the Vifor Second Amended Agreement, CSL Vifor agreed that it would not sell or otherwise supply vadadustat until the FDA has granted regulatory approval for vadadustat for the treatment of anemia due to CKD in adult patients with DD-CKD in the Territory and until CSL Vifor has entered a supply agreement with the applicable member of the Supply Group.

Similar to the Vifor First Amended Agreement, the Vifor Second Amended Agreement is structured as a profit share arrangement between the Company and CSL Vifor in which the Company will receive approximately 66% of the profit, net of certain pre-specified costs. Under the Vifor Second Amended Agreement, CSL Vifor made an upfront payment to the Company of $25.0 million in lieu of the previously disclosed milestone payment of $25.0 million that CSL Vifor was to pay the Company following approval of vadadustat by the FDA, as established under the Vifor First Amended Agreement.

Unless earlier terminated, the Vifor Second Amended Agreement will expire upon the later of the expiration of all patents that claim or cover vadadustat or expiration of marketing or regulatory exclusivity for vadadustat in the Territory. CSL Vifor may terminate the Vifor Second Amended Agreement in its entirety upon 30 months' prior written notice after the first anniversary

of the receipt of regulatory approval, if approved from the FDA for vadadustat for dialysis-dependent CKD patients. The Company may terminate the Vifor Second Amended Agreement in its entirety for convenience, following the earlier of a certain period of time elapsing or following certain specified regulatory events, and upon six months' prior written notice. If the Company so terminates for convenience, subject to specified exceptions, the Company will pay a termination fee to CSL Vifor. In addition, either party may, subject to a cure period, terminate the Vifor Second Amended Agreement in the event of the other party's uncured material breach or bankruptcy.

Investment Agreement

In connection with the Vifor Agreement, in May 2017, the Company and CSL Vifor entered into an investment agreement, or the First Investment Agreement, pursuant to which the Company sold an aggregate of 3,571,429 shares of the Company's common stock, or the 2017 Shares, to CSL Vifor 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.

CSL Vifor agreed to a lock-up restriction such that it agreed not to sell the 2017 Shares for a period of time following the effective date of the First Investment Agreement as well as a customary standstill agreement. In addition, the First Investment Agreement contains voting agreements made by CSL Vifor with respect to the 2017 Shares. The 2017 Shares have not been registered pursuant to the Securities Act of 1933, as amended, or 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.

In connection with entering into the Vifor Second Amended Agreement, on February 18, 2022, the Company and CSL Vifor entered into an investment agreement, or the Second Investment Agreement, pursuant to which the Company sold an aggregate of 4,000,000 shares of its common stock, or the 2022 Shares, to CSL Vifor for a total of $20 million on February 22, 2022. The amount representing the premium over the grant date fair value on the date of the transaction, $13.6 million, was determined by the Company to represent the consideration related to the Vifor Second Amended Agreement. CSL Vifor has agreed to a lock-up restriction to not sell or otherwise dispose of the 2022 Shares for a period of time following the effective date of the Second Investment Agreement as well as a customary standstill agreement. In addition, the Second Investment Agreement contains voting agreements made by CSL Vifor with respect to the 2022 Shares. The 2022 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/or Rule 506 promulgated thereunder, as the transaction did not involve any public offering within the meaning of Section 4(a)(2) of the Securities Act. A more detailed description of the Vifor Second Amended Agreement and the Company's evaluation of this agreement under ASC 606 can be found in Note 4 of the Notes to the Consolidated Financial Statements in the 2022 Annual Report on Form 10-K.

Revenue Recognition

The Company identified one performance obligation in connection with its obligations under the Vifor Second Amended Agreement, which is the License Deliverable, or License Performance Obligation. The transaction price at inception was comprised of: (i) the up-front payment of $25.0 million, (ii) the premium paid by CSL Vifor on the First Investment Agreement of $4.7 million, and (iii) the premium paid by CSL Vifor on the Second Investment Agreement of $13.6 million. Pursuant to the terms of the Vifor Second Amended Agreement, these payments from CSL Vifor are non-refundable and non-creditable against any other amount due to the Company. Also pursuant to the Vifor Second Amended Agreement, if the Centers for Medicare & Medicaid Services, or CMS, determines that vadadustat is excluded from the Transitional Drug Add-on Payment Adjustment, or TDAPA, the Company can terminate the Vifor Second Amended Agreement and will be required to repay the up-front payment and the premiums paid by CSL Vifor in the First Investment Agreement and Second Investment Agreement, respectively. CSL Vifor also agreed that it will not sell or otherwise supply vadadustat until the FDA has granted regulatory approval for vadadustat for the treatment of anemia due to CKD in adult patients with DD-CKD . The Company constrains the variable consideration to an amount for which a significant revenue reversal is not probable. Therefore, the Company determined that the entire transaction price at inception was constrained under ASC 606, and the Company has recorded the transaction price to deferred revenue as of March 31, 2023.

Refund Liability to Customer

Pursuant to the Vifor Second Amended Agreement, CSL Vifor contributed $40.0 million to a working capital fund established to partially fund the Company's costs of purchasing vadadustat from its contract manufacturers, or the Working Capital Fund, which amount of funding will fluctuate, and which funding the Company is required to repay to CSL Vifor over time. The $40 million initial contribution to the Working Capital Fund represents 50% of the amount of purchase orders that the Company has placed with its contract manufacturers for the supply of vadadustat for the Territory already delivered as of the effective

date of the Vifor Second Amended Agreement, and to be delivered through the end of 2023. The amount of the Working Capital Fund will be reviewed at specified intervals and is adjusted based on a number of factors including outstanding supply commitments for vadadustat for the Territory and agreed upon vadadustat inventory levels held by the Company for the Territory. Upon termination or expiration of the Vifor Second Amended Agreement for any reason other than convenience by CSL Vifor (including following receipt of the CRL for vadadustat), the Company will be required to refund the outstanding balance of the Working Capital Fund on the date of termination or expiration.

The Company has recorded the Working Capital Fund as a refund liability under ASC 606. The Company has determined that the refund liability itself does not represent an obligation to transfer goods or services to CSL Vifor in the future. The Company has therefore determined that this refund liability is not a contract liability under ASC 606. The Company accounted for the refund liability as a debt arrangement with zero coupon interest. The Company imputed interest on the refund liability to the customer at a rate of 15.0% per annum, which was determined based on certain factors, including the Company's credit rating, comparable securities yield, and the expected repayment period of the Working Capital Fund. The Company recorded an initial discount on the refund liability to the customer and a corresponding deferred gain to the refund liability to customer on the condensed consolidated balance sheet as of the date the funds were received from CSL Vifor, which was March 18, 2022. The discount on the note payable is being amortized to interest expense using the effective interest method over the expected term of the refund liability. The deferred gain is being amortized to interest income on a straight-line basis over the expected term of the refund liability. The amortization of the discount was $0.8 million and immaterial for the three months ended March 31, 2023 and 2022, respectively. The amortization of the deferred gain was $1.0 million and immaterial for the three months ended March 31, 2023 and 2022, respectively. As of March 31, 2023, the $40.8 million total refund liability is classified as a long-term refund liability based on management's estimate of potential amounts that could be refundable exceeding a one-year period.

License Agreement with Panion & BF Biotech, Inc.

The Company had a license agreement, which was amended from time to time, with Panion & BF Biotech, Inc., or Panion, under which Keryx, the Company's wholly owned subsidiary, was the contracting party, or the Panion License Agreement, pursuant to which Keryx in-licensed the exclusive worldwide rights, excluding certain Asian-Pacific countries, or the Licensor Territory, for the development and commercialization of ferric citrate.

On April 17, 2019, the Company and Panion entered into a second amended and restated license agreement, or the Panion Amended License Agreement, which amends and restates in full the Panion License Agreement, effective as of April 17, 2019. The Panion Amended License Agreement provides Keryx with an exclusive license under Panion-owned know-how and patents with the right to sublicense, develop, make, use, sell, offer for sale, import and export ferric citrate worldwide, excluding the Licensor Territory. The Panion Amended License Agreement also provides Panion with an exclusive license under the Keryx-owned patents, with the right to sublicense (with the Company’s written consent), develop, make, use, sell, offer for sale, import and export ferric citrate in certain countries in the Licensor Territory. Under the Panion Amended License Agreement, Panion is eligible to receive from the Company or any sublicensee royalty payments based on a mid-single digit percentage of sales of ferric citrate in the Company’s licensed territories. The Company is eligible to receive from Panion or any sublicensee royalty payments based on a mid-single digit percentage of net sales of ferric citrate in Panion’s licensed territories. A more detailed description of this license agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the 2022 Annual Report on Form 10-K.

The Company recognized royalty payments due to Panion of approximately $2.6 million and $2.5 million during the three months ended March 31, 2023 and 2022, respectively, relating to the Company’s sales of Auryxia in the United States and JT and Torii’s net sales of Riona in Japan, as the Company is required to pay a mid-single digit percentage of net sales of ferric citrate in the Company’s licensed territories to Panion under the terms of the Panion Amended License Agreement.

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

The Company has an Amended and Restated Sublicense Agreement, which was amended in June 2013, with JT and Torii, or the JT and Torii Sublicense Agreement, under which Keryx, the Company’s 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 hydrate in Japan. JT and Torii are responsible for the future development and commercialization costs in Japan. A more detailed description of this sublicense agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the 2022 Annual Report on Form 10-K.

The Company identified two performance obligations in connection with its obligations under the JT and Torii Sublicense Agreement: (i) *License and Supply Performance Obligation* and (ii) *Rights to Future Know-How Performance Obligation*. The Company allocated 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.

The Company recognized license revenue of $1.1 million during each of the three months ended March 31, 2023 and 2022 related to royalties earned on net sales of Riona in Japan. The Company records the associated mid-single digit percentage of net sales royalty expense due to Panion, the licensor of Riona, in the same period as the royalty revenue from JT and Torii is recorded.

License Agreement with Averoa SAS

On December 22, 2022, the Company and Averoa SAS, or Averoa, entered into a license agreement, or the Averoa License Agreement, pursuant to which the Company granted to Averoa an exclusive license to develop and commercialize ferric citrate, or the Licensed Product, in the European Economic Area, Turkey, Switzerland and the United Kingdom, or the Averoa Territory.

Under the Averoa License Agreement, the Company is entitled to receive tiered, escalating royalties ranging from a mid-single digit percentage to a low double-digit percentage of Averoa's annual net sales in the Averoa Territory, including certain minimum royalty amounts in certain years, and subject to reduction in certain circumstances. The Company and Averoa will establish a joint steering committee to oversee the development, manufacturing and commercialization of the Licensed Product in the Averoa Territory. The Averoa License Agreement expires on the date of expiration of all royalty obligations due thereunder with respect to the Licensed Product on a country-by-country basis in the Averoa Territory, unless earlier terminated in accordance with the agreement.

The Averoa License Agreement provides that the Company and Averoa will enter into a supply agreement pursuant to which the Company will supply the Licensed Product to Averoa for commercial use in the Averoa Territory. The Company will have the right to terminate the supply agreement upon 24 months' notice, which may be provided on or after January 1, 2024. The Company did not receive any consideration under this agreement as of March 31, 2023. A more detailed description of this license agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the 2022 Annual Report on Form 10-K.

5. Liability Related to Sale of Future Royalties

On February 25, 2021, the Company entered into the Royalty Agreement with HCR, pursuant to which the Company sold to HCR its right to receive royalties and sales milestones for vadadustat in Japan and certain other Asian countries, such countries, collectively, the MTPC Territory, and such payments collectively the Royalty Interest Payments, in each case, payable to the Company under the MTPC Agreement, subject to an annual maximum "cap" of $13.0 million, or the Annual Cap, and an aggregate maximum "cap" of $150.0 million, or the Aggregate Cap. The Company received $44.8 million from HCR (net of certain transaction expenses) under the Royalty Agreement. The Company retains the right to receive all potential future regulatory milestones for vadadustat under the MTPC Agreement. Although the Company sold its right to receive royalties and sales milestones for vadadustat in the MTPC Territory as described above, as a result of its ongoing involvement in the cash flows related to these royalties, the Company will continue to account for these royalties as revenue. The Company recognized the proceeds received from HCR as a liability that is being amortized using the effective interest method over the life of the arrangement. At the transaction date, the Company recorded the net proceeds of $44.8 million as a liability. In order to determine the amortization of the liability, the Company is required to estimate the total amount of future net royalty payments to be made to HCR over the term of the Royalty Agreement. The total threshold of net royalties to be paid, less the net proceeds received, will be recorded as interest expense over the life of the liability. The Company imputes interest on the unamortized portion of the liability using the effective interest method. The annual effective interest rate as of March 31, 2023 was 0% which is reflected as interest expense in the unaudited condensed consolidated statements of operations and comprehensive loss. On a quarterly basis, the Company reassesses the effective interest rate and adjusts the rate prospectively as needed. A more detailed description of Royalty Agreement can be found in Note 6 of the Notes to the Consolidated Financial Statements in the 2022 Annual Report on Form 10-K.

The following table shows the activity within the liability account for the three months ended March 31, 2023:

	March 31, 2023 (in thousands)
Liability related to sale of future royalties, beginning balance at December 31, 2022	$ 57,484
MTPC royalties payable	(425)
Liability related to sale of future royalties, ending balance	$ 57,059

6. Fair Value of Financial Instruments

Based on the fair value hierarchy, the Company classifies its cash equivalents within Level 1 or Level 2. This is because the Company values its cash equivalents 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 March 31, 2023 and December 31, 2022 are summarized below:

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
March 31, 2023				
Assets:				
Cash and cash equivalents	$ 56,953	$ —	$ —	$ 56,953
	$ 56,953	$ —	$ —	$ 56,953
Liabilities:				
Derivative liability	$ —	$ —	$ 760	$ 760
	$ —	$ —	$ 760	$ 760

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
December 31, 2022				
Assets:				
Cash and cash equivalents	$ 90,466	$ —	$ —	$ 90,466
	$ 90,466	$ —	$ —	$ 90,466
Liabilities:				
Derivative liability	$ —	$ —	$ 760	$ 760
	$ —	$ —	$ 760	$ 760

The Company's Loan Agreement with Pharmakon (see Note 10) contains certain provisions that change the underlying cash flows of the debt instrument, including a potential extension to the interest-only period dependent on both (i) no event of default having occurred and continuing and (ii) the Company achieving certain regulatory and revenue conditions. One of the regulatory conditions was approval of vadadustat by August 2022, however, in March 2022, the Company received the CRL from the FDA stating that the FDA had determined that it could not approve the NDA for vadadustat in its present form. Therefore, the Company is no longer eligible for the interest-only extension period and this no longer changes the underlying cash flows of the debt instrument. The Company also assessed the acceleration of the obligations under the Loan Agreement under certain events of default. In addition, under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. In accordance with ASC 815, the Company concluded that these features are not clearly and closely related to the host instrument, and represent a single compound derivative that is required to be re-measured at fair value on a quarterly basis.

The potential events of default assessed include failure to maintain, on an annual basis, a minimum liquidity threshold which started in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia which started in the fourth quarter of 2020. The Company recorded a derivative liability related to the Company's Loan Agreement with Pharmakon of $0.8 million as of March 31, 2023 and December 31, 2022. The Company classified the derivative liability as a non-current liability on the

unaudited condensed consolidated balance sheet as of March 31, 2023 and December 31, 2022. The estimated fair value of the derivative liability on both March 31, 2023 and December 31, 2022 was determined using a scenario-based approach and discounted cash flow model that includes principal and interest payments under various scenarios involving clinical development success for vadadustat and various cash flow assumptions. The Company used a 0% probability of clinical development success due to receipt of the CRL from the FDA for vadadustat. Should the Company's assessment of the probabilities around these scenarios change, including for changes in market conditions, there could be a change to the fair value of the derivative liability.

The following table provides a roll-forward of the fair value of the derivative liability (in thousands):

Balance at December 31, 2022	$	760
Change in fair value of derivative liability, recorded as other income		—
Balance at March 31, 2023	$	760

The Company had no other assets or liabilities measured at fair value on a recurring basis using significant unobservable inputs (Level 3) at March 31, 2023 and December 31, 2022.

7. Inventory

The components of inventory are summarized as follows:

	March 31, 2023	December 31, 2022
	(in thousands)	
Raw materials	$ 503	$ 610
Work in process	8,100	8,086
Finished goods	12,504	13,676
Total inventory	$ 21,107	$ 22,372

Long-term inventory, which primarily consists of raw materials and work in process, is included in other assets in the Company's unaudited condensed consolidated balance sheets.

	March 31, 2023	December 31, 2022
	(in thousands)	
Balance Sheet Classification:		
Inventory	$ 20,604	$ 21,762
Other assets	503	610
Total inventory	$ 21,107	$ 22,372

Inventory amounts written down as a result of excess, obsolescence, scrap or other reasons and charged to cost of goods sold totaled $0.3 million and $5.3 million during the three months ended March 31, 2023 and 2022, respectively. The decrease in inventory amounts written down for the three months ended March 31, 2023 as compared to the three months ended March 31, 2022 was primarily due to lower write-downs to inventory reserves related to expired inventory. Inventory write-downs are recorded as a component of cost of goods sold in the unaudited condensed consolidated statement of operations.

8. Intangible Assets and Goodwill

Intangible Assets

The following table presents the Company's intangible assets at March 31, 2023 and December 31, 2022 (in thousands):

	March 31, 2023		
	Gross Carrying Value	Accumulated Amortization	Total
Intangible assets:			
Developed product rights for Auryxia	$ 213,603	$ (150,529)	$ 63,074
Total	$ 213,603	$ (150,529)	$ 63,074

	December 31, 2022		
	Gross Carrying Value	Accumulated Amortization	Total
Intangible assets:			
Developed product rights for Auryxia	$ 213,603	$ (141,519)	$ 72,084
Total	$ 213,603	$ (141,519)	$ 72,084

The Company amortizes its definite-lived intangible assets using the straight-line method, which is considered the best estimate of economic benefit, over its estimated useful life of six years. The Company recorded $9.0 million in amortization expense related to the developed product rights for Auryxia during each of the three months ended March 31, 2023 and 2022.

Goodwill

The Company's goodwill results from the acquisition of Keryx in December 2018. Goodwill was $55.1 million as of March 31, 2023 and December 31, 2022. The Company operates in one operating segment which the Company considers to be the only reporting unit. Goodwill is evaluated for impairment at the reporting unit level on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that it is more likely than not that the fair value of the reporting unit is less than its carrying amount. Events that could indicate impairment and trigger an interim impairment assessment include, but are not limited to, an adverse change in current economic or market conditions, including a significant prolonged decline in market capitalization, a significant adverse change in legal factors, unexpected adverse business conditions, and an adverse action by a regulator. During the three months ended March 31, 2023, the Company evaluated business factors, including the Company's market capitalization as impacted by the continued decline in the Company's stock price and the Company's negative carrying value as of March 31, 2023 to determine if there were events or changes in circumstance to indicate that the fair value of the reporting unit was less than its carrying value. The Company performed a qualitative interim impairment assessment of the Company's goodwill balance as of the three months ended March 31, 2023. The Company determined that it was not more likely than not that the fair value of the reporting unit was less than its carrying value and, therefore, did not perform a further quantitative interim impairment test for any period.

The Company's qualitative assessments were based on the Company's estimates and assumptions, a number of which are dependent on external factors and actual results may differ materially from these estimates. In addition, the future occurrence of events including, but not limited to, an adverse change in current economic and market conditions, including a significant prolonged decline in market capitalization, a significant adverse change in legal factors, unexpected adverse business conditions and an adverse action or assessment by a regulator could indicate potential impairment and trigger an interim impairment assessment of goodwill, which could result in an impairment of goodwill. As a result of the significance of goodwill, the Company's results of operations and financial position in a future period could be negatively impacted should an impairment test be triggered that results in an impairment of goodwill.

9. Accrued Expenses

Accrued expenses as of March 31, 2023 and December 31, 2022 are as follows:

	March 31, 2023	December 31, 2022
	(in thousands)	
Product revenue allowances	$ 22,368	$ 29,005
Accrued clinical	1,148	5,755
Accrued payroll and related	5,717	11,481
Lease liability	5,160	4,744
Royalties	2,636	3,804
Professional fees	1,621	1,734
Accrued commercial manufacturing	1,299	4,310
Accrued restructuring	1,286	2,751
Accrued other	5,132	7,413
Total accrued expenses	$ 46,367	$ 70,997

10. Debt

Term Loans

On November 11, 2019, the Company, with Keryx as guarantor, entered into a loan agreement, or the Loan Agreement, with BioPharma Credit PLC as collateral agent and a lender, or the Collateral Agent, and BioPharma Credit Investments V (Master) LP as a lender, pursuant to which term loans in an aggregate principal amount of $100.0 million were made available to the Company in two tranches, subject to certain terms and conditions, or the Term Loans. BioPharma Credit PLC subsequently transferred its interest in the Term Loans, solely in its capacity as a lender, to its affiliate, BPCR Limited Partnership. The Collateral Agent and the lenders are collectively referred to as Pharmakon. The first tranche of $80.0 million, or Tranche A, was drawn on November 25, 2019, or the Tranche A Funding Date, and the second tranche of $20.0 million, or Tranche B, was drawn on December 10, 2020, or the Tranche B Funding Date. Each of the Tranche A Funding Date and the Tranche B Funding Date, a Funding Date. The Tranche A draw was $77.3 million, net of facility fee, other expenses incurred by Pharmakon and reimbursed by the Company, or Lender Expenses, and issuance costs. The Tranche B draw was $20.0 million, net of immaterial Lender Expenses and issuance costs.

Proceeds from the Term Loans may be used for general corporate purposes. The Company and Keryx entered into a Guaranty and Security Agreement with the Collateral Agent, or the Guaranty and Security Agreement, on the Tranche A Funding Date. Pursuant to the Guaranty and Security Agreement, the Company's obligations under the Term Loans are unconditionally guaranteed by Keryx, or the Guarantee. Additionally, the obligations of the Company and Keryx under the Term Loans and the Guarantee are secured by a first priority lien on certain assets of the Company and Keryx, including Auryxia and certain related assets, cash, and certain equity interests held by the Company and Keryx, collectively the Collateral.

The Term Loans bear interest at a floating rate per annum equal to the three-month LIBOR rate plus 7.50%, subject to a 2.00% LIBOR floor and a 3.35% LIBOR cap, payable quarterly in arrears. The Term Loans will mature on the fifth anniversary of the Tranche A Funding Date, or the Maturity Date. The Company is required to repay the principal under the Term Loans in equal quarterly payments starting on the 33rd-month anniversary of the applicable Funding Date, or the Amortization Schedule. During the three months ended March 31, 2023, the Company made two quarterly principal payments under the Term Loans totaling $16.0 million. Under certain circumstances, unless certain liquidity conditions are met, the Maturity Date may decrease by up to one year, and the Amortization Schedule may correspondingly commence up to one year earlier.

The Loan Agreement permits voluntary prepayment at any time in whole or in part, subject to a prepayment premium. The prepayment premium would be 2.00% of the principal amount being prepaid prior to the third anniversary of the applicable Funding Date, 1.00% on or after the third anniversary, but prior to the fourth anniversary, of the applicable Funding Date, and 0.50% on or after the fourth anniversary of the applicable Funding Date but prior to the Maturity Date, and a make-whole premium on or prior to the second anniversary of the applicable Funding Date in an amount equal to foregone interest through the second anniversary of the applicable Funding Date. A change of control triggers a mandatory prepayment of the Term Loans.

The Loan Agreement contains customary representations, warranties, events of default and covenants of the Company and its subsidiaries, including maintaining, on an annual basis, a minimum liquidity threshold which started in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia which started in the fourth quarter of 2020. On February 18, 2022, the Loan Agreement was amended by the First Amendment and Waiver, which waived the provision under the Loan Agreement that required the Company to not be subject to any qualification as a going concern within the Company's 2021 Annual Report on

Form 10-K. Pursuant to the First Amendment and Waiver, the Company's filings of Form 10-Q for fiscal quarters ending June 30, 2022 and September 30, 2022, and its future Annual Reports on Form 10-K, must not be subject to any qualification as to going concern, which requirement as to the Company's filings on Form 10-Q was waived in the Second Amendment and Waiver. If the Company does not satisfy the covenant as to going concern in any of these filings, the Company will be in default under the Loan Agreement. If an event of default occurs and is continuing under the Loan Agreement, the Collateral Agent is entitled to take enforcement action, including acceleration of amounts due under the Loan Agreement. Under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. As of March 31, 2023 and December 31, 2022, the Company determined that no events of default had occurred.

On July 15, 2022, or the Effective Date, the Company and Pharmakon entered into the Second Amendment and Waiver, or the Second Amendment and Waiver, which amended and waived certain provisions of the Loan Agreement, as amended by the First Amendment and Waiver.

Pursuant to the Second Amendment and Waiver, on the Effective Date, the Company made a $5.0 million prepayment of the principal of the tranche A loan, or the Second Amendment Effective Date Tranche A Prepayment, and a $20.0 million prepayment of principal of the tranche B loan, or the Second Amendment Effective Date Tranche B Prepayment, in each case, together with any and all accrued and unpaid interest on such prepayments of principal to the Effective Date. In connection therewith, the Company also paid $0.5 million in prepayment premiums under the Loan Agreement. During the three months ended September 30, 2022, the Company recorded a debt extinguishment loss of $0.9 million. A more detailed description of Second Amendment and Waiver can be found in Note 11 of the Notes to the Consolidated Financial Statements in the 2022 Annual Report on Form 10-K.

The Company assessed the terms and features of the Loan Agreement in order to identify any potential embedded features that would require bifurcation or any beneficial conversion feature. As part of this analysis, the Company assessed the economic characteristics and risks of the Loan Agreement, including put and call features. The terms and features assessed include a potential extension to the interest-only period dependent on both no event of default having occurred and continuing and the Company achieving certain regulatory and revenue conditions. The Company also assessed the acceleration of the obligations under the Loan Agreement under an event of default. In addition, under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. In accordance with ASC 815, the Company concluded that these features are not clearly and closely related to the host instrument, and represent a single compound derivative that is required to be re-measured at fair value on a quarterly basis.

The fair value of the derivative liability related to the Company’s Loan Agreement with Pharmakon was $0.8 million as of March 31, 2023 and December 31, 2022. The Company classified the derivative liability as a non-current liability on the unaudited condensed consolidated balance sheet as of March 31, 2023.

The Company recognized interest expense related to the Loan Agreement of $1.8 million and $2.7 million during the three months ended March 31, 2023 and 2022, respectively.

11. Stockholders’ Equity

Authorized and Outstanding Capital Stock

On June 5, 2020, the Company filed a Certificate of Amendment to its Ninth Amended and Restated Certificate of Incorporation, or its Charter, to increase the number of authorized shares of common stock from 175,000,000 to 350,000,000. As of March 31, 2023, the authorized capital stock of the Company included 350,000,000 shares of common stock, par value $0.00001 per share, of which 185,835,946 and 184,135,714 shares were issued and outstanding as of March 31, 2023 and December 31, 2022, respectively; and 25,000,000 shares of undesignated preferred stock, par value $0.00001 per share, of which no shares were issued and outstanding as of March 31, 2023 and December 31, 2022.

At-the-Market Facility

On March 12, 2020, the Company filed a prospectus supplement relating to the Company's sales agreement with Cantor Fitzgerald & Co., or the Prior Sales Agreement, pursuant to which it was able to offer and sell up to $65.0 million of its common stock at current market prices from time to time.

On February 25, 2021, the Company filed a prospectus relating to the Prior Sales Agreement with its new shelf registration statement (which replaced the prior shelf registration statement and the sales agreement prospectus supplement), pursuant to which it was able to offer and sell up to $100.0 million of its common stock at current market prices from time to time. On

March 1, 2022, the Company filed a prospectus relating to the Prior Sales Agreement, pursuant to which it was authorized to offer and sell up to $25.3 million of its common stock at current market prices from time to time. On March 16, 2022, the Company terminated the Prior Sales Agreement. During the three months ended March 31, 2022, the Company sold 404,600 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $0.8 million.

On April 7, 2022, the Company entered into an Open Market Sale Agreement℠, or the Sales Agreement, with Jefferies LLC, or Jefferies, as agent, for the offer and sale of common stock at current market prices in amounts to be determined from time to time. Also, on April 7, 2022, the Company filed a prospectus supplement relating to the Sales Agreement, pursuant to which it is able to offer and sell under the Sales Agreement up to $26.0 million of its common stock at current market prices from time to time. From the date of filing of the prospectus supplement through the date of the filing of this Quarterly Report on Form 10-Q, the Company has not sold any shares of its common stock under this program.

Equity Plans

The Company maintains one stock incentive plan, the 2014 Incentive Plan, or the 2014 Plan, as well as the 2014 Employee Stock Purchase Plan, or the 2014 ESPP. The 2014 Plan replaced the Company's Amended and Restated 2008 Equity Incentive Plan, or 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. On June 6, 2019, the Company's stockholders approved the Amended and Restated 2014 Employee Stock Purchase Plan, or the ESPP. The Company also maintains an inducement award program that is separate from the Company's equity plans under which inducement awards may be granted consistent with Nasdaq Listing Rule 5635(c)(4). During the three months ended March 31, 2023, the Company granted 22,000 options to purchase shares of the Company's common stock to new hires as inducements material to such employees' entering into employment with the Company, of which 22,000 options remained outstanding as of March 31, 2023.

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 1 of each calendar year, by an amount equal to three percent (3%) of the number of the Company's outstanding shares on a fully diluted basis as of the close of business on the immediately preceding December 31, or the 2014 Plan Evergreen Provision. The Company's Board of Directors may act prior to January 1 of any year to provide that there will be no automatic increase in the number of Akebia 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, or the Merger, whereby Keryx Biopharmaceuticals, Inc., or Keryx, became a wholly owned subsidiary of the Company, the Company assumed outstanding and unexercised options to purchase Keryx's stock, 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 granted 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.

The Company grants annual service-based stock options to employees and directors and SARs to certain executives under the 2014 Plan. During the three months ended March 31, 2023, the Company issued 2,489,500 options to employees under the 2014 Plan. During the three months ended March 31, 2023, the Company issued 635,313 SARs to one executive under the 2014 Plan. 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 and SARs granted by the Company generally 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 and SARs generally 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 and SARs generally expire 10 years after the date of grant.

The Company also grants performance-based stock options to employees under the 2014 Plan. The Company issued no performance-based stock options under the 2014 Plan during the three months ended March 31, 2023. The performance-based stock options granted by the Company generally vest in connection with the achievement of specified commercial, regulatory and corporate milestones. The performance-based stock options also generally feature a time-based vesting component. 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 options granted and recognized over time based on the probability of meeting such commercial, regulatory and corporate milestones.

The Company also grants annual service-based restricted stock units, or RSUs, to employees and directors under the 2014 Plan. The Company also occasionally issues RSUs not in connection with the annual grant process to employees and directors. During the three months ended March 31, 2023, the Company issued 2,459,675 RSUs to employees and no RSUs to directors under the 2014 Plan. Generally, RSUs granted by the Company vest in one of the following ways: (i) 100% of each RSU grant vests on the first anniversary of the grant date, (ii) one third of each RSU grant vests on the first, second and third anniversaries of the grant date, (iii) 50% of each RSU grant vests on the first anniversary and 25% of each RSU grant vests every six months after the one year anniversary of the grant date, or (iv) one third of each RSU grant vests on the first anniversary and the remaining two thirds vests in eight substantially equal quarterly installments beginning after the one year anniversary, 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 also grants performance-based restricted stock units, or PSUs, to employees under the 2014 Plan. The Company issued no PSUs during the three months ended March 31, 2023. The PSUs granted by the Company generally vest in connection with the achievement of specified commercial, regulatory and corporate milestones. The PSUs also generally feature a time-based vesting component. 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 over time based on the probability of meeting such commercial, regulatory and corporate milestones.

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. As noted above, the Company's stockholders approved the ESPP, which amended and restated the Company's 2014 ESPP, on June 6, 2019. As of March 31, 2023, the maximum aggregate number of shares of the Company's common stock available for future issuance under the ESPP is 4,734,495. Under the ESPP, each offering period is six months, at the end of which employees who elect to 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. The Company issued 103,500 shares under the ESPP during the three months ended March 31, 2023.

12. 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 November 2020, 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 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 the Company 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, which commenced in September 2019. In November 2020, the Company entered into a Sixth Amendment to the Cambridge Lease, or the Sixth Amendment, to extend the term of the Cambridge Lease with respect to the lab space from November 30, 2021 to January 31, 2025. The Sixth Amendment includes two months of free rent starting in December 2020 and additional monthly lease payments of approximately $48,000, which commenced in December 2021, and is subject to annual rent escalations, which commenced in December 2022.

Additionally, the Company has a lease for 27,300 square feet of office space in Boston, Massachusetts, or the Boston Lease. The total monthly lease payments under the initial base rent were approximately $136,000 and are subject to annual rent escalations. In February 2022, the Company entered into the First Amendment to the Boston Lease, or the First Lease Amendment, to extend the term of the Boston Lease from February 2023 to July 2031. The First Lease Amendment includes five months of free rent starting in March 2023 and monthly lease payments of $200,122 commencing on August 1, 2023, with an annual rent escalation of approximately 2% commencing on August 1, 2024. The First Lease Amendment also includes a landlord's allowance for certain leasehold improvements to the premises in an amount of up to $1,954,680, provided that such allowance must be used prior to August 1, 2024.

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 Boston Lease office space expires on July 31, 2031, with an extension option for one additional five-year term available. The renewal options in these real estate leases were not included in the calculation of the operating lease assets and operating lease liabilities as the renewal is not reasonably certain. The term of the Cambridge Lease with respect to the lab space expires on January 31, 2025, with an extension option for one additional period through September 11, 2026. The renewal option in this real estate lease was included in the calculation of the operating lease assets and operating lease liabilities as the renewal is reasonably certain. The lease agreements do not contain residual value guarantees. Operating lease costs were $1.8 million for each of the three months ended March 31, 2023 and 2022. Cash paid for amounts included in the measurement of operating lease liabilities was $1.7 million and $1.8 million for the three months ended March 31, 2023 and 2022, respectively.

In September 2019, Keryx entered into an agreement to sublease the Boston office space to Foundation Medicine, Inc., or Foundation. The sublease was subject and subordinate to the Boston Lease between Keryx and the landlord. The term of the sublease commenced on October 16, 2019, upon receipt of the required consent from the landlord for the sublease agreement, and expired on February 27, 2023. Foundation was obligated to pay Keryx rent that approximated the rent due from Keryx to its landlord with respect to the Boston Lease. Sublease rental income is recorded to other income. Keryx was obligated for all payment terms pursuant to the Boston Lease, and the Company guaranteed Keryx's obligations under the sublease. Keryx recorded $0.3 million and $0.5 million in sublease rental income from Foundation during the three months ended March 31, 2023 and 2022, respectively.

The Company has not entered into any material short-term leases or financing leases as of March 31, 2023.

The total security deposit in connection with the Cambridge Lease is $1.6 million as of March 31, 2023. Additionally, the Company recorded $1.1 million for the security deposit under the Boston Lease. The Cambridge Lease and the Boston Lease have their security deposits in the form of a letter of credit, all of which are included as restricted cash in prepaid expenses and other current assets in the Company's unaudited condensed consolidated balance sheets as of March 31, 2023.

As of March 31, 2023, undiscounted minimum rental commitments under non-cancelable leases, for each of the next five years and total thereafter are as follows:

	Operating Lease Payments
Remaining 2023	$ 5,248
2024	8,162
2025	8,289
2026	6,132
2027	$ 2,570
Thereafter	$ 9,631
Total	$ 40,032

In arriving at the operating lease liabilities, the Company applied incremental borrowing rates ranging from 6.65% to 7.25%, which were based on the remaining lease term at either the date of adoption of ASC 842 or the effective date of any subsequent lease term extensions. As of March 31, 2023, the remaining lease terms ranged from 3.45 years to 8.34 years. As of March 31, 2023, the following represents the difference between the remaining undiscounted minimum rental commitments under non-cancelable leases and the operating lease liabilities:

	Operating Leases
	(in thousands)
Undiscounted minimum rental commitments	$ 40,032
Present value adjustment using incremental borrowing rate	(7,452)
Operating lease liabilities	$ 32,580

Manufacturing Agreements

As a result of the Merger, the Company's contractual obligations 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 Manufacture and Supply Agreement with BioVectra and the Amended and Restated Product Manufacture and Supply and Facility Construction Agreement with BioVectra, the Company agreed to purchase minimum quantities of Auryxia drug substance annually at predetermined prices as well as reimburse BioVectra for certain costs in connection with construction of a new facility for the manufacture and supply of Auryxia drug substance.

On December 22, 2022, the Company and BioVectra entered into the BioVectra Termination Agreement, pursuant to which the parties agreed, among other things, to terminate, effective immediately, any and all existing agreements entered into between the parties in connection with the manufacture and supply, by BioVectra to the Company, of Auryxia drug substance. Under the terms of the BioVectra Termination Agreement, each of the Company and BioVectra have released one another from all existing and future claims and liabilities and the return of certain materials and documents. Furthermore, as it relates to all open purchase orders, BioVectra is relieved from any obligations to manufacture any product or perform services under any such open purchase orders, and the Company is relieved from any obligations to purchase any product under such open purchase orders. The Company is also relieved from any obligations to pay any outstanding invoices related to performance by BioVectra of services and all other obligations under the agreements. In addition, the Company agreed to pay BioVectra a total of $32.5 million consisting of (i) an upfront payment of $17.5 million and (ii) six quarterly payments of $2.5 million commencing in April 2024, totaling $15.0 million. The upfront payment of $17.5 million was made during the quarter ended December 31, 2022 and was recognized to cost of goods sold. In accordance with ASC 420, Exit or Disposal Cost Obligations, the Company recognized a liability and corresponding expense for the remaining termination fees based on estimated fair value as of December 22, 2022, or the BioVectra Effective Date. The Company imputed interest on the liability for the remaining termination fees at a rate of 17.0% per annum, which was determined based on certain factors, including the Company's credit rating, comparable securities yield, and expected repayment period of the remaining termination fees. The Company recorded an initial discount on the remaining termination fees on the consolidated balance sheet as of the BioVectra Effective Date. This resulted in the recording of a liability and corresponding charge to cost of goods sold of $11.2 million during the quarter ended December 31, 2022. The discount on the liability balance is being amortized to interest expense using the effective interest rate method over the term of the liability. The amortization of the discount was $0.5 million for the three months ended March 31, 2023.

Pursuant to the Master Manufacturing Services and Supply Agreement between the Company and Siegfried, as amended (the most recent amendment having been executed on February 28, 2023), or the Siegfried Agreement, the Company has agreed to purchase a minimum quantity of drug substance of Auryxia at a predetermined price. The term of the Siegfried Agreement expires on December 31, 2024, unless otherwise agreed by the parties and subject to the Company's option to extend the term through December 31, 2026 by providing 12 months' prior written notice to Siegfried. The Siegfried Agreement provides the Company and Siegfried with certain early termination rights. As of March 31, 2023, the Company is required to purchase a minimum quantity of drug substance for Auryxia annually at a total cost of approximately $23.9 million through the end of 2024.

On April 9, 2019, the Company entered into a Supply Agreement with Esteve Química, S.A., or Esteve, or the Esteve Agreement. The Esteve Agreement included the terms and conditions under which Esteve would manufacture vadadustat drug substance for commercial use. Pursuant to the Esteve Agreement, the Company provided rolling forecasts to Esteve on a quarterly basis, or the Esteve Forecast. The Esteve Forecast reflected the Company's needs for vadadustat drug substance produced by Esteve over a certain number of months, represented as a quantity of vadadustat drug substance per calendar quarter. The parties agreed to a volume-based pricing structure under the Esteve Agreement. On December 16, 2022, the Company, MTPC, and Esteve executed the Assignment Agreement, pursuant to which the Supply Agreement between the Company and Esteve was assigned to MTPC. The Assignment Agreement transferred the rights and obligations of the Supply Agreement to MTPC, specifically including the obligations under certain purchase orders issued by the Company and accepted by Esteve. As such, the Company will have no further obligation to take delivery of or pay for product delivered by Esteve under the transferred Esteve Agreement and the purchase orders.

On March 11, 2020, the Company entered into a Supply Agreement with Patheon Inc., or Patheon, or the Patheon Agreement. The Patheon Agreement includes the terms and conditions under which Patheon will manufacture vadadustat drug product for commercial use. Pursuant to the Patheon Agreement, the Company provides Patheon a long-term forecast on an annual basis, as well as short-term forecasts on a quarterly basis, or the Patheon Forecast. The Patheon Forecast reflects the Company's needs for commercial supply of vadadustat drug product produced by Patheon, represented as a quantity of drug product per calendar quarter. The parties have agreed to a volume-based pricing structure under the Patheon Agreement. The Patheon Agreement has an initial term beginning March 11, 2020 and ending June 30, 2023 and automatically renews for successive one-year terms unless either party gives the other party eighteen months' prior written notice. The current term of the Patheon Agreement ends June 30, 2025. Pursuant to the Patheon Agreement, the Company has agreed to purchase a certain percentage of the global demand for vadadustat drug product from Patheon. As of March 31, 2023, the Company had a minimum commitment with Patheon for $3.1 million through the third quarter of 2023.

On April 2, 2020, the Company entered into a Supply Agreement with STA Pharmaceutical Hong Kong Limited, a subsidiary of WuXi AppTec, or WuXi STA, as amended on April 15, 2021, or the WuXi STA DS Agreement. The WuXi STA DS Agreement includes the terms and conditions under which WuXi STA will manufacture vadadustat drug substance for commercial use. Pursuant to the WuXi STA DS Agreement, the Company provides rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DS Forecast. The WuXi STA DS Forecast reflects the Company's needs for vadadustat drug substance produced by WuXi STA over a certain number of quarters. The parties have agreed to a volume-based pricing structure under the WuXi STA DS Agreement. The WuXi STA DS Agreement has an initial term of four years, beginning April 2, 2020 and ending April 2, 2024. Pursuant to the WuXi STA DS Agreement, the Company has agreed to purchase a certain percentage of the global demand for vadadustat drug substance from WuXi STA. As of March 31, 2023, the Company has committed to purchase $15.3 million of vadadustat drug substance from WuXi STA through the end of 2023.

On February 10, 2021, the Company entered into a Supply Agreement with WuXi STA, or the WuXi STA DP Agreement. The WuXi STA DP Agreement includes the terms and conditions under which WuXi STA will manufacture and supply vadadustat drug product for commercial purposes. Pursuant to the WuXi STA DP Agreement, the Company will provide rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DP Forecast. Each WuXi STA DP Forecast will reflect the quantities of vadadustat drug product that the Company expects to order from WuXi STA over a certain number of months, represented as a quantity of vadadustat drug product per calendar quarter. Pursuant to the WuXi STA DP Agreement, the Company has agreed to purchase a certain percentage of global demand for vadadustat drug product from WuXi STA. The parties have agreed to a volume-based pricing structure under the WuXi STA DP Agreement. The vadadustat drug product price will remain fixed for the first 12 months and thereafter shall be annually reviewed by the Company and WuXi STA. The Company will also reimburse WuXi STA for certain reasonable expenses. The WuXi STA DP Agreement has an initial term of four years, beginning February 10, 2021 and ending February 10, 2025. The WuXi STA DP Agreement may be renewed or extended by mutual agreement of the Company and WuXi STA with at least 18 months' prior written notice. The WuXi STA DP Agreement allows the Company to terminate the relationship on 180 calendar days' prior written notice to WuXi STA for any reason. In addition, each party has the ability to terminate the WuXi STA DP Agreement upon the occurrence of certain conditions.

Other Third-Party Contracts

The Company contracts with various organizations to conduct research and development activities with remaining contract costs to the Company of approximately $77.6 million at March 31, 2023. 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.

Litigation and Related Matters

From time to time, the Company may become subject to legal proceedings and claims which arise in the ordinary course of its business. Consistent with ASC 450, *Contingencies*, the Company's policy is to record a liability if a loss in a significant legal dispute is considered probable and an amount can be reasonably estimated. The Company provides disclosure when a loss in excess of any reserve is reasonably possible, and if estimable, the Company discloses the potential loss or range of possible loss. Significant judgment is required to assess the likelihood of various potential outcomes and the quantification of loss in those scenarios. The Company's estimates change as litigation progresses and new information comes to light. Changes in Company estimates could have a material impact on the Company's results and financial position. As of March 31, 2023, the Company does not have any significant legal disputes that require a loss liability to be recorded. The Company continually monitors the need for a loss liability for litigation and related matters.

13. Net Loss per Share

For purposes of the diluted net loss per share calculation, preferred stock, stock options, restricted stock, RSUs and SARs are considered to be common stock equivalents and have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented in the unaudited condensed consolidated statement of operations and comprehensive loss. 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:

	As of March 31,	
	2023	2022
Outstanding stock options and SARs	14,113,067	14,187,899
Unvested restricted stock units	6,460,421	5,782,635
Total	20,573,488	19,970,534

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following information should be read in conjunction with our unaudited condensed consolidated financial statements and related notes included in this Quarterly Report on Form 10-Q and our Annual Report on Form 10-K for the year ended December 31, 2022 filed with the U.S. Securities and Exchange Commission, or the SEC, on March 10, 2023, or the 2022 Annual Report on Form 10-K, including the audited consolidated financial statements and related notes therein. This discussion and analysis contains forward-looking statements that involve significant risks and uncertainties. As a result of many factors, such as those set forth under "Risk Factors" in Part II, Item 1A. of this Quarterly Report on Form 10-Q, our actual results may differ materially from those anticipated in these forward-looking statements.

Business Overview

We are a fully integrated biopharmaceutical company committed to addressing patients' unmet needs. Since our initial public offering in 2014, we have built a business focused on developing and commercializing innovative therapeutics that we believe serves as a foundation for future growth. Our purpose is to better the life of each person impacted by kidney disease, and we have established ourselves as a leader in the kidney community. We believe our demonstrated ability to deliver value broadly to the kidney community has enabled us to build a sustainable company. While our current focus centers on people living with kidney disease, we believe our continued commitment to our products and pipeline assets, focusing on all patients who can realize a meaningful benefit from our medicines, will result in delivering value for shareholders.

Our current portfolio includes:

- ***Auryxia® (ferric citrate)***, a medicine approved and marketed in the United States for two indications: (1) the control of serum phosphorus levels in adult patients with dialysis dependent chronic kidney disease, or DD-CKD, or the Hyperphosphatemia Indication, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with non-dialysis-dependent chronic kidney disease, or NDD-CKD. The product is also available in Japan and Taiwan.
- ***Vafseo™ (vadadustat)***, an oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor, is approved in Europe for the treatment of symptomatic anemia due to chronic kidney disease, or CKD, in adult patients on chronic maintenance dialysis. Vadadustat is also approved in Japan for the treatment of anemia due to CKD in adult patients on dialysis and not on dialysis. Additionally, vadadustat is approved in Korea as an anemia treatment for patients with CKD on hemodialysis. Vadadustat is also under regulatory review for the treatment of anemia due to CKD in Australia, Taiwan and other countries. We continue to pursue a path to potentially gain approval for vadadustat in the U.S. Further, we have several lifecycle management and indication expansion opportunities currently under evaluation or in development for vadadustat.
- ***HIF-PH inhibitors*** in preclinical development. The discovery of hypoxia-inducible factor, or HIF, laid the foundation to explore the central role of oxygen sensing in many diseases. As we have seen through the development of vadadustat as a treatment for anemia due to CKD, when stabilized, HIF triggers wide-ranging adaptive, protective responses during hypoxic or ischemic conditions. Our clinical team and research scientists are eager to further develop HIF-PH inhibitors for various indications including acute kidney injury, or AKI, and retinopathy of prematurity, or ROP.

We continue to explore additional commercial and development opportunities to expand our pipeline and portfolio of novel therapeutics through both internal research and external innovation to leverage our fully integrated team.

Auryxia

Today we market Auryxia in the United States with our well-established, nephrology-focused commercial organization. Auryxia is a non-calcium, non-chewable, orally administered tablet that was approved for marketing by the U.S. Food and Drug Administration, or 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 treatment of iron deficiency anemia, and was commercially launched for this indication in the United States shortly thereafter. Our Japanese sublicensee, Japan Tobacco, Inc., or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize ferric citrate hydrate as Riona® in Japan. Averoa SAS, or Averoa, has an exclusive license to develop and commercialize ferric citrate in the European Economic Area, or EEA, Turkey, Switzerland and the United Kingdom.

Vadadustat

We are seeking regulatory approval in the United States for vadadustat as an oral treatment of anemia in adult DD-CKD patients. We and Mitsubishi Tanabe Pharma Corporation, or MTPC, are also seeking regulatory approval for vadadustat as a treatment for anemia in adult DD-CKD and NDD-CKD patients in the United Kingdom, Switzerland and Australia, and Taiwan, respectively.

In April 2023, the European Commission, or EC, approved the marketing authorization of vadadustat under the trade name Vafseo™ for the treatment of symptomatic anemia associated with CKD in adults on chronic maintenance dialysis, which is applicable to all 27 European Union member states and Iceland, Norway and Liechtenstein. Following the termination of our U.S. and international collaboration agreements with Otsuka in June 2022, we regained full rights to vadadustat in Europe, Australia, China, Canada, Latin America, the Middle East and Russia. As we do not have a commercial presence in Europe, we are seeking a partner in Europe and will support the partner's launch of vadadustat. We are seeking to identify and secure a partner that can effectively facilitate treatment of as many people as would benefit from vadadustat, thus maximizing the value of the asset.

We submitted a New Drug Application, or NDA, to the FDA for vadadustat in March of 2021. On March 29, 2022, the FDA issued a complete response letter, or CRL, to our NDA for vadadustat. The FDA concluded that the data in the NDA do not support a favorable benefit-risk assessment of vadadustat for dialysis and non-dialysis patients. The FDA expressed safety concerns noting failure to meet non-inferiority in MACE in the non-dialysis patient population, the increased risk of thromboembolic events, driven by vascular access thrombosis in dialysis patients, and the risk of drug-induced liver injury. We believe there are compelling data supporting a positive benefit-risk profile for the use of vadadustat broadly in patients with CKD, including non-dialysis patients though we have always remained cautious about receiving a broad label for vadadustat that would extend to non-dialysis patients with anemia due to CKD. As such, we began the process to dispute the FDA ruling, and in October 2022, we submitted a Formal Dispute Resolution Request, or FDRR, with the FDA regarding the CRL, specifically related to DD-CKD adult patients. The appeal focused on the favorable balance of the benefits and risks of vadadustat for the treatment of adult DD-CKD patients in light of safety concerns expressed by the FDA in the CRL related to the rate of adjudicated thromboembolic events driven by vascular access thrombosis for vadadustat compared to the active comparator and the risk of drug-induced liver injury. In February 2023, we received a second interim response from the FDA to the FDRR. In March 2023, we had a productive meeting with the FDA, who indicated that it was continuing internal consultation with experts to complete the review and render a decision. The FDA has indicated that it has completed internal discussions, and we expect a response to the FDRR within the next thirty days.

Following the termination of our collaboration agreement with Otsuka Pharmaceutical Co. Ltd., or Otsuka, we own full rights to vadadustat in the U.S., subject to our licensing agreement with CSL Vifor. If we obtain FDA approval of vadadustat for DD-CKD adult patients, we plan to commercialize vadadustat in the United States with CSL Vifor.

Leveraging our learnings from the research and development of vadadustat, and a breadth of scientific expertise on the HIF pathway, we believe there is potential to leverage HIFs to treat other hypoxic conditions and to explore the use of HIFs in acute settings. We believe this potential applies to vadadustat as well as other preclinical assets we are internally developing.

Regarding broader uses of vadadustat, in July 2020 we partially funded an investigator-sponsored clinical trial conducted by The University of Texas Health Science Center at Houston, or UTHealth, in Houston, Texas, evaluating the use of vadadustat as a potential therapy to prevent and treat acute respiratory distress syndrome, or ARDS, in adult patients who have been hospitalized due to COVID-19 and hypoxemia (O2 saturation ≤94%). The study was a phase 2, randomized, double-blind, placebo-controlled trial that measured the proportion of patients who had scores of 6, 7, or 8 on the National Institute of Allergy and Infectious Disease Ordinal Scale, or NIAID-OS, at Day 7 and Day 14, with Day 14 being the primary endpoint. While the study missed the primary endpoint, the data, detailed in the Clinical Development Program section, were encouraging. For reference, subjects receiving vadadustat demonstrated 94% probability for conferring benefit on the NIAID-OS at Day 14, slightly below the primary superiority threshold of >95% probability. We believe vadadustat has the potential to prevent the worsening of ARDS more broadly since the mechanism underlying the benefits are not specific to COVID-19, and we will further explore vadadustat in an acute care setting.

Operating Overview

We have incurred net losses in each year since inception. Our net losses were $26.2 million and $62.4 million for the three months ended March 31, 2023 and 2022, respectively. Substantially all of our net losses resulted from costs incurred in connection with the continued commercialization of Auryxia and development efforts relating to vadadustat, including conducting clinical trials of, and seeking regulatory approval for, vadadustat, providing general and administrative support for these operations and protecting our intellectual property.

Our ability to achieve profitability depends in part on our ability to manage our expenses. Following receipt of the CRL, in April 2022 and May 2022, we implemented a reduction of our workforce by approximately 42% across all areas of our company including several members of management (47% inclusive of the closing of the majority of open positions). These actions reflect our determination to refocus our strategic priorities around our commercial product, Auryxia®, and our development portfolio, and are steps in a cost savings plan to significantly reduce our expense profile. On November 7, 2022, we implemented a further reduction in workforce by approximately 14% consisting solely of individuals within the commercial organization as a result of our decision to shift to a strategic account management focused model for our commercial efforts.

We expect to continue to incur additional operating expenses, including additional research and development expenses to our pipeline, additional costs related to vadadustat, and research and development and selling, general and administrative expenses for ongoing development and commercialization of Auryxia, which could lead to operating losses for the foreseeable future. In addition to any additional costs not currently contemplated due to the events associated with or resulting from the workforce reductions noted above, our ability to achieve profitability and our financial position will depend, in part, on the rate of our future expenditures, on our product revenue from Auryxia, our collaboration revenue, our ability to successfully implement cost avoidance measures and reduce overhead costs and our ability to obtain additional funding. We expect to continue to incur significant expenses if and as we:

- continue our commercialization activities for Auryxia and vadadustat, if we are able to obtain marketing approval for vadadustat following receipt of the CRL from the FDA in March 2022, and any other product or product candidate, including those that may be in-licensed or acquired;
- address the issues identified in the CRL for vadadustat that we received from the FDA and pursue our appeal of the CRL for vadadustat with the FDA;
- conduct and enroll patients in any clinical trials, including post-marketing studies or any other clinical trials for Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired;
- seek marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired;
- maintain marketing approvals for Auryxia and vadadustat, if we are able to obtain marketing approval for vadadustat following receipt of the CRL from the FDA in March 2022, and any other product, including those that may be in-licensed or acquired;
- manufacture Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, for commercial sale and clinical trials;
- conduct discovery and development activities for additional product candidates or platforms that may lead to the discovery of 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 and commercialize other product candidates and technologies;
- continue to repay, and pay any associated pre-payment penalties, if applicable, the senior secured term loans in an aggregate principal amount of $51.0 million as of March 31, 2023, or the Term Loans, that were made available to us pursuant to the loan agreement that we entered into with funds managed by Pharmakon Advisors LP, or Pharmakon, in November 2019, or the Loan Agreement;
- make royalty, milestone or other payments under our license agreements and any future license agreements;
- maintain, protect and expand our intellectual property portfolio;
- make decisions with respect to our personnel, including the retention of key employees;
- make decisions with respect to our infrastructure, including to support our operations as a fully integrated publicly traded biopharmaceutical company; and
- experience any additional delays or encounter issues with any of the above.

We have not generated, and may not generate, enough product revenue 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 contract research organizations, or CROs, to carry out our clinical development activities. If we obtain marketing approval for vadadustat, and as we continue to commercialize Auryxia, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We expect to finance future cash needs through product revenue, potential strategic transactions, public or private equity or debt transactions, or a combination of these approaches. If we are unable to raise additional capital in sufficient amounts when needed or on attractive terms, we may not be

able to pursue development and commercial activities related to Auryxia and vadadustat, if approved, or any additional products and product candidates, including those that may be in-licensed or acquired. Any of these events could significantly harm our business, financial condition and prospects.

From inception through March 31, 2023, we raised approximately $793.5 million of net proceeds from the sale of equity, including $519.8 million from various underwritten public offerings, $223.7 million from at-the-market offerings, or ATM offerings, pursuant to prior sales agreements with Cantor Fitzgerald & Co., and $70.0 million from the sale of 7,571,429 shares of common stock to CSL Vifor. As of March 31, 2023, through our collaboration agreement with MTPC and our prior collaboration agreements with Otsuka we received approximately $837.1 million in cost-share funding, and are not entitled to receive any additional cost-share funding. On June 30, 2022, we entered into the Termination and Settlement Agreement, or the Termination Agreement, with Otsuka, pursuant to which we received a nonrefundable and non-creditable payment of $55.0 million in consideration for the covenants and agreements set forth in the Termination Agreement.

On November 11, 2019, we entered into the Loan Agreement pursuant to which term loans in an aggregate principal amount of $100.0 million were made available to us in two tranches, subject to certain terms and conditions, or the Term Loans. On July 15, 2022, or the Effective Date, we entered into the Second Amendment and Waiver with BioPharma Credit PLC, or the Collateral Agent, BPCR Limited Partnership, as a Lender, and BioPharma Credit Investments V (Master) LP, as a Lender, or the Second Amendment and Waiver, which amends and waives certain provisions of the Loan Agreement as amended by the First Amendment and Waiver between the Collateral Agent, the Lenders and us, dated February 18, 2022. The Collateral Agent and the Lenders are collectively referred to as Pharmakon. Pursuant to the Second Amendment and Waiver, we made prepayments totaling $25.0 million together with a prepayment premium of $0.5 million plus all accrued and unpaid interest on such prepayments of principal to the Effective Date, and Pharmakon agreed to waive or modify certain covenants in the Loan Agreement. In addition, on February 25, 2021, we received an upfront payment of $44.8 million (net of certain transaction expenses) in connection with our sale to HealthCare Royalty Partners IV, L.P., or HCR, of the right to receive all royalties and sales milestones payable to us under our collaboration agreement with MTPC, or the MTPC Agreement, subject to certain caps and other terms and conditions described elsewhere in this Quarterly Report on Form 10-Q. Finally, on February 18, 2022, we entered into a Second Amended and Restated License Agreement, or the Vifor Second Amended Agreement, with CSL Vifor. Pursuant to the Vifor Second Amended Agreement, CSL Vifor made an upfront payment to us of $25.0 million in lieu of the previously disclosed milestone payment of $25.0 million that CSL Vifor was to pay to us following approval of vadadustat by the FDA. Also pursuant to the Vifor Second Amended Agreement, Vifor contributed $40 million to a working capital fund established to partially fund our costs of purchasing vadadustat from our contract manufacturers, or the Working Capital Fund, which amount of funding will fluctuate, and which funding we are required to repay to CSL Vifor over time.

Financial Overview

Revenue

To date, our revenues have been derived from product revenue from commercial sales of Auryxia, collaboration revenues, which include license and milestone payments, royalty and cost-sharing revenue generated through collaboration and license agreements with partners for the development and commercialization of vadadustat, a nonrefundable, non-creditable termination fee pursuant to the terms of the Termination Agreement with Otsuka, and royalty revenue from sales of Riona in Japan.

We expect our revenue to continue to be generated primarily from our commercial sales of Auryxia, our collaborations with MTPC and Japan Tobacco, Inc., and its subsidiary, Torii Pharmaceutical Co., Ltd., collectively JT and Torii, and any other collaborations into which we have entered or may enter. We will not recognize any future revenue pursuant to our former collaborations with Otsuka.

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, changes in our excess purchase commitment liability, and royalties due to the licensor of Auryxia related to U.S. and Japan product sales recognized during the period. Cost of goods sold also includes costs to manufacture drug product provided to MTPC for commercial sale of Vafseo in Japan.

As a result of the merger whereby Keryx Biopharmaceuticals, Inc., or Keryx, became a wholly owned subsidiary of ours, and the application of purchase accounting, costs of goods sold also includes both amortization expense and, if applicable, impairment charges associated with the fair value of the developed product rights for Auryxia. The fair value of the developed product rights for Auryxia is being amortized over its estimated useful life, which as of March 31, 2023 is estimated to be six years.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the development of vadadustat, 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 CROs and investigative sites that conduct our clinical trials;
- the cost of acquiring, developing and manufacturing clinical trial materials through CMOs;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies;
- costs associated with preclinical, clinical and regulatory activities; and
- costs associated with pre-launch inventory build for vadadustat in the United States and Europe, for which we received the CRL from the FDA in the United States in March 2022.

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 trials of Auryxia and vadadustat or if, when, or to what extent we will receive marketing approval for vadadustat or generate revenue from the commercialization and sale of vadadustat, if approved. We may never succeed in achieving marketing approval for vadadustat.

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

From inception through March 31, 2023, we have incurred $1.6 billion in research and development expenses. We expect to incur significant research and development expenditures for the foreseeable future as we continue the development of Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired.

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 trials, and drug substance and drug product manufacturing for clinical trials.

In 2020, we completed our global Phase 3 clinical program for vadadustat to which the majority of our research and development costs are attributable. A significant portion of our research and development costs have been external costs, which we track on a program-by-program basis. These external costs include fees paid to investigators, consultants, central laboratories and CROs in connection with our clinical trials, and costs related to acquiring and manufacturing clinical trial materials. Our internal research and development costs are primarily personnel-related costs, depreciation and other indirect costs. We do not track our internal research and development expenses on a program-by-program basis as they are deployed across multiple projects under development.

The following table summarizes our external research and development expenses by program, as well as expenses not allocated to programs, for the three months ended March 31, 2023 and 2022:

	Three Months Ended March 31,	
	2023	2022
	(in thousands)	
Vadadustat external costs	$ 6,440	$ 17,153
External costs for other programs	2,475	6,353
Total external research and development expenses	8,915	23,506
Headcount, consulting, facilities and other	10,771	20,327
Total research and development expenses	$ 19,686	$ 43,833

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.

Results of Operations

Comparison of the Three Months Ended March 31, 2023 and 2022

	Three Months Ended		Increase
	March 31, 2023	March 31, 2022	(Decrease)
	(in thousands)		
Revenues:			
Product revenue, net	$ 34,828	$ 41,448	$ (6,620)
License, collaboration and other revenue	5,299	20,251	(14,952)
Total revenues	40,127	61,699	(21,572)
Cost of goods sold:			
Product	10,473	22,333	(11,860)
Amortization of intangibles	9,011	9,011	—
Total cost of goods sold	19,484	31,344	(11,860)
Operating expenses:			
Research and development	19,686	43,833	(24,147)
Selling, general and administrative	25,221	44,327	(19,106)
License expense	568	688	(120)
Restructuring	106	—	106
Total operating expenses	45,581	88,848	(43,267)
Operating loss	(24,938)	(58,493)	33,555
Other expense, net	(1,279)	(3,928)	2,649
Net loss	$ (26,217)	$ (62,421)	$ 36,204

Product Revenue, Net. Net product revenue is derived from sales of our only commercial product in the United States, Auryxia. We distribute our product principally through a limited number of wholesale distributors as well as certain specialty pharmacy providers. Net product revenue was $34.8 million for the three months ended March 31, 2023, compared to $41.4 million for the three months ended March 31, 2022. The decrease was primarily due to a reduction in inventory of Auryxia by certain customers as well as a decline in volume, partially offset by a higher net price per tablet.

License, Collaboration and Other Revenue. License, collaboration and other revenue was $5.3 million for the three months ended March 31, 2023, compared to $20.3 million for the three months ended March 31, 2022. The decrease was primarily due to a reduction in revenue from the Otsuka collaboration agreement because on June 30, 2022, we and Otsuka entered into the Termination Agreement, which, among other things, terminated the cost sharing arrangement under the Otsuka collaboration

agreement for the United States, or the Otsuka U.S. Agreement, and the Otsuka collaboration agreement for certain territories outside the United States, or the Otsuka International Agreement. We will not recognize any future revenue under the Otsuka U.S. Agreement or the Otsuka International Agreement. Additionally, on December 16, 2022, we, MTPC, and Esteve Química, S.A., or Esteve, executed an Assignment of Supply Agreement, or the Assignment Agreement, pursuant to which the supply agreement between us and Esteve, or the Esteve Agreement, was assigned to MTPC. The Assignment Agreement transferred the rights and obligations of the Esteve Agreement to MTPC, including the obligations under certain purchase orders issued by us and accepted by Esteve. Therefore, we expect significantly less revenue in the future under our supply agreement with MTPC.

Cost of Goods Sold - Product. Cost of goods sold of $10.5 million for the three months ended March 31, 2023 consisted of costs associated with the manufacturing of Auryxia and supply of Vafseo to MTPC for commercial sale in Japan and $0.3 million related to excess and obsolescence reserves associated with inventory.

Cost of goods sold of $22.3 million for the three months ended March 31, 2022 consisted of costs associated with the manufacturing of Auryxia and supply of Vafseo to MTPC for commercial sale in Japan, and $5.3 million related to excess and obsolescence reserves associated with Auryxia partially offset by a $0.8 million reduction to the liability for excess purchase commitments.

Cost of Goods Sold - Amortization of Intangibles. Amortization of intangibles relates to the acquired developed product rights for Auryxia, which is being amortized using a straight-line method over its estimated useful life of approximately six years. Amortization of intangibles during each of the three months ended March 31, 2023 and 2022 was $9.0 million.

Research and Development Expenses. Research and development expenses were $19.7 million for the three months ended March 31, 2023, compared to $43.8 million for the three months ended March 31, 2022, a decrease of $24.1 million. The decrease was primarily due to the following:

	(in millions)
Vadadustat development expenses	$ (10.7)
Headcount, consulting, facilities and other	(13.4)
Total net decrease	$ (24.1)

The decrease in research and development expense was primarily due to decreased headcount related costs as a result of the April 2022 reduction in force, decreased outsourced contract services, and decreased clinical trial costs and development expenses related to vadadustat. Although we expect our research and development expenses to continue to decrease in the near term, we will continue to incur significant research and development expenses in future periods in support of ongoing or planned studies with respect to Auryxia and vadadustat and development of other potential product candidates.

Selling, General and Administrative Expenses. Selling, general and administrative expenses were $25.2 million for the three months ended March 31, 2023, compared to $44.3 million for the three months ended March 31, 2022. The decrease of $19.1 million was primarily due to decreased headcount related costs as a result of the 2022 reductions in force and lower marketing expenses following receipt of the CRL for vadadustat.

License Expenses. License expense related to royalties due to Panion relating to sales of Riona in Japan were $0.6 million for the three months ended March 31, 2023, compared to $0.7 million for the three months ended March 31, 2022.

Restructuring. Restructuring expenses were $0.1 million for the three months ended March 31, 2023. There were no restructuring expenses for the three months ended March 31, 2022.

Other Expense, Net. Other expense, net, was $1.3 million for the three months ended March 31, 2023, compared to $3.9 million for the three months ended March 31, 2022. The decrease of $2.6 million was primarily due to a decrease in interest expense as a result of principal prepayments totaling $25.0 million made on the Term Loans pursuant to the Second Amendment and Waiver in the year ended December 31, 2022, as well as an additional $24.0 million of quarterly principal payments made on the Term Loans pursuant to the Loan Agreement with Pharmakon, reducing our outstanding balance on the Term Loans. The decrease was also related to a decrease in non-cash interest expense from our liability for the sale of future royalties due to a decrease in the effective interest rate on the liability for the three months ended March 31, 2023, compared to the three months ended March 31, 2022.

Liquidity and Capital Resources

We have funded our operations principally through sales of our common stock, payments received from our collaboration partners, product sales, debt, a royalty transaction, and a refund liability to a customer. As of March 31, 2023, we had cash and cash equivalents of approximately $57.0 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. On April 7, 2022, we entered into an Open Market Sale Agreement℠, or the Sales Agreement, with Jefferies LLC, or Jefferies, as agent, for the offer and sale of common stock at current market prices in amounts to be determined from time to time. Also, on April 7, 2022, we filed a prospectus supplement relating to the Sales Agreement, pursuant to which we are able to offer and sell under the Sales Agreement up to $26.0 million of our common stock at current market prices from time to time. From the date of filing of the prospectus supplement through the date of the filing of this Quarterly Report on Form 10-Q, we have not sold any shares of our common stock under this program. As of March 31, 2023, through our collaboration agreements with Otsuka and MTPC we received approximately $837.1 million in cost-share funding, and are not entitled to receive any additional cost-share funding.

Cash Flows

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

	Three Months Ended	
	March 31, 2023	March 31, 2022
	(in thousands)	
Net cash (used in) provided by:		
Operating activities	$ (17,538)	$ (21,620)
Investing activities	—	(114)
Financing activities	(15,966)	47,545
Net (decrease) increase in cash, cash equivalents, and restricted cash	$ (33,504)	$ 25,811

Operating Activities. Net cash used in operating activities was $17.5 million for the three months ended March 31, 2023 as compared to $21.6 million for the three months ended March 31, 2022. The decrease in cash used was primarily a result of lower net loss driven by decreased operating expenses, including payroll related expenses, as well as lower payments for inventory and lower accounts receivable. This was partially offset by decreases in accounts payable and accrued expenses.

Investing Activities. No net cash was used in investing activities for the three months ended March 31, 2023. Net cash used in investing activities for the three months ended March 31, 2022 was $0.1 million and was primarily comprised of purchases of equipment.

Financing Activities. Net cash used in financing activities for the three months ended March 31, 2023 primarily consisted of principal payments of debt of $16.0 million.

Net cash provided by financing activities for the three months ended March 31, 2022 was $47.5 million and consisted of net proceeds from a refund liability to a customer of $40.0 million, net proceeds from the issuance of common stock of $7.2 million, and proceeds from the sale of stock under our employee stock purchase plan.

Operating Capital Requirements

We have one product, Auryxia, approved for commercial sale in the United States. While we expect to be able to generate positive cash flows from our existing operations, we have not generated, and may not generate, enough product revenue from the sale of Auryxia to realize net profits from product sales. We currently have exclusive rights under a series of patents and patent applications to commercialize Auryxia in the U.S. that currently protect us from generic drug competition until March 2025. Following loss of exclusivity in the U.S., we may not be able realize enough product revenue from sales of Auryxia to realize net profits from product sales after March 2025. We have incurred losses and cumulative negative cash flows from operations in each year since our inception in February 2007, and as of March 31, 2023, we had an accumulated deficit of $1.6 billion. Our current operating plan anticipates continued increasing levels of cash flows from operations. We expect to continue to incur additional research and development expenses related to our pipeline, additional costs related to vadadustat, and research and development and selling, general and administrative expenses for our ongoing development and commercialization of Auryxia.

We expect our cash resources to fund our current operating plan for at least twelve months from the date of this filing. We expect to finance future cash needs through product revenue, potential strategic transactions, public or private equity or debt transactions, expense management, or a combination of these approaches. We plan to reduce our need for future financing through product sales, expense management, and cost avoidance measures in line with being a single commercial product company. We believe that the execution of further cost avoidance measures, future decisions by the FDA or foreign regulatory agencies related to the potential regulatory approval of vadadustat, and our ability to generate additional value from vadadustat, if approved, through partnerships or other strategic transactions could potentially further extend our cash runway for a period greater than twelve months. However, these future decisions and transactions are not contemplated in our operating plan and are outside of our control. Additionally, with loss of exclusivity, or LOE, for Auryxia in March of 2025, we believe the Centers for Medicare & Medicaid Services, or CMS, decision to include phosphate binders in the dialysis bundle could potentially lead to higher sales of Auryxia after the LOE date than in other LOE scenarios, and plan to work with payors and providers to continue the use of Auryxia beyond LOE. Assuming we are successful in those endeavors, we will require additional funding to fund our strategic growth beyond Auryxia or to pursue later stage development and commercial activities for our product candidates and any additional product or product candidates, including those that may be in-licensed or acquired.

There can be no assurance that the current operating plan will be achieved in the time frame anticipated by us, or that our cash resources will fund our operating plan for the period of time anticipated by us, or that additional funding will be available on terms acceptable to us, or at all. 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 numerous risks and uncertainties, and actual results could vary as a result of a number of factors, many of which are outside our control. 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. If our operating performance deteriorates significantly from the levels expected in our operating plan, it could have an effect on our liquidity and our ability to continue as a going concern in the future. Our future funding requirements, both near- and long-term, will depend on many factors including, but not limited to, those described under Part II, Item 1A. Risk Factors under the heading "Risks Related to our Financial Position, Need for Additional Capital and Growth Strategy."

Contractual Obligations

As of March 31, 2023, other than as disclosed in Note 10 and Note 12 to our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q, there have been no material changes to our contractual obligations and commitments from those described under “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in our 2022 Annual Report on Form 10-K.

Critical Accounting Estimates and Significant Judgments

Our management’s discussion and analysis of our financial condition and results of operations are based on our unaudited condensed consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these unaudited condensed 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 unaudited condensed consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue, inventory, our excess purchase commitment liability, liabilities related to sale of future royalties, refund liabilities to customers, impairment of intangible assets and income taxes. 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. In making estimates and judgments, management employs critical accounting policies.

During the three months ended March 31, 2023, there were no material changes to our critical accounting estimates as reported in our 2022 Annual Report on Form 10-K.

Item 3. Quantitative and Qualitative Disclosures about Market Risk.

We are exposed to market risk related to changes in interest rates. As of March 31, 2023 and December 31, 2022, we had cash and cash equivalents of $57.0 million and $90.5 million, respectively, consisting primarily of money market mutual funds consisting of certificates of deposit and corporate debt securities. Interest rate sensitivity is affected by changes in the general level of U.S. interest rates, particularly because our investments are 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.

In addition, we are exposed to market risk related to exchange rates. A portion of our revenues for the three months ended March 31, 2023 was received in royalty payments converted to U.S. dollars based on the net sales of Riona and Vafseo™ in

Japanese yen. Our exchange rate risk arises from such foreign currency net sales. As a result, we are exposed to movements in the exchange rates of the Japanese yen against the U.S. dollar.

For the royalty payments we received based on net sales of Riona and Vafseo in Japan for the three months ended March 31, 2023, a 5.0% appreciation or depreciation of the Japanese yen against the U.S. dollar would have increased or decreased, respectively, our revenues in the three months ended March 31, 2023 by approximately $0.1 million.

We have generally accepted the exposure to exchange rate movements without using derivative financial instruments to manage this foreign currency risk.

Item 4. Controls and Procedures.

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 Securities Exchange Act of 1934, as amended, or 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 Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding required disclosure.

As of March 31, 2023, our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), 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. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer have concluded as of March 31, 2023, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act, during the three months ended March 31, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

Legal Proceedings Relating to Vadadustat

Opposition Proceedings Against Akebia

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

On July 26, 2022, Sandoz AG filed an opposition against our issued European Patent No. 3277270 in the European Patent Office.

On February 13, 2023, FibroGen, Inc., or FibroGen, filed an opposition against our issued European Patent No. 3357911 in the European Patent Office.

Proceedings Filed by Akebia Against FibroGen, Inc.

Japan

In 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 certain of FibroGen's HIF-related patents in Japan: JP4845728, JP5474872 and JP5474741. On September 26, 2019, the JPO conducted an invalidation trial for JP5474872 and JP4845728. On November 11, 2019, the JPO conducted an invalidation trial for JP5474741. On April 1, 2022, the JPO issued a final decision for JP4845728, which invalidated all claims except claims directed to the medical use to treat anemia that does not respond to erythropoiesis. On May 18, 2022, the JPO issued a final decision for JP5474741 and JP5474872, which maintained the claims in amended form. In May 2022, MTPC filed revocation lawsuits for the three patents in the Intellectual Property High Court requesting cancellation of the JPO's decisions. In July 2022, we filed a revocation lawsuit for JP4845728 in the Intellectual Property High Court requesting cancellation of the JPO's decision. In August 2022, we filed revocation lawsuits for JP5474741 and JP5474872 in the Intellectual Property High Court requesting cancellation of the JPO's decisions. In September 2022, FibroGen filed a revocation lawsuit for JP4845728 in the Intellectual Property High Court requesting cancellation of the JPO's decision on the claims that were invalidated. We do not believe the JPO's decisions will prevent our collaboration partner MTPC from continuing to commercialize vadadustat for the treatment of anemia due to CKD in Japan.

United Kingdom

On December 13, 2018, we filed Particulars of Claim in the Patents Court of the United Kingdom to challenge the validity of FibroGen'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). In May 2019, Astellas Pharma Inc., or Astellas, the exclusive licensee of FibroGen's HIF-related patents, sued Akebia for patent infringement in the Patents Court of the UK. In September 2019, we filed an Amended Particulars of Claim to include FibroGen's European Patent No. 1487472, or the '472 EP Patent (UK). On February 28, 2020, the parties agreed to dismiss the '472 EP Patent (UK) from the trial.

A trial was conducted in March 2020. On April 20, 2020, the Patents Court of the UK issued a judgment in favor of Akebia, which invalidated all the claims at issue in each of the '823 EP Patent (UK), the '333 EP Patent (UK), the '153 EP Patent (UK), the '155 EP Patent (UK) and the '301 EP Patent (UK). The '531 EP Patent (UK) was amended to a single claim to recite one specific compound; this claim was held to be valid but not infringed by vadadustat. On June 11, 2020, FibroGen and Astellas appealed the Patents Court's judgment on the invalidity of the '823 EP Patent (UK), the '301 EP Patent (UK), the '333 EP Patent (UK), the '153 EP Patent (UK), and the '155 EP Patent (UK) in the Court of Appeal (Civil Division). On June 8, 2021 - June 10, 2021, the United Kingdom Court of Appeal held a three-day hearing for the appeal. On August 24, 2021, the Court of Appeal issued a judgment, which reversed the Patents Court's judgment on the invalidity of the '823 EP Patent (UK) and maintained certain claims of the '823 EP Patent (UK) and the '301 EP Patent (UK) in amended form, and which affirmed the Patents Court's judgment on the invalidity of the '333 EP Patent (UK), the '155 EP Patent (UK), and the '153 EP Patent (UK). Akebia sought permission to appeal to the UK Supreme Court, which was granted on October 3, 2022. Hearing for the appeal is scheduled for March 5-7, 2024. We do not expect the UK Court of Appeal's judgment to have any effect on our commercialization of vadadustat in the UK because the patents expired in December 2022.

Legal Proceedings Relating to Auryxia

ANDA Litigation

In February 2023, Keryx Biopharmaceuticals, Inc., or Keryx, received a Paragraph IV certification notice letter regarding an Abbreviated New Drug Application, or ANDA, submitted to the U.S. Food and Drug Administration, or FDA by Zydus Worldwide DMCC, or Zydus, requesting approval for a generic version of Auryxia tablets (210 mg ferric iron per tablet). On March 24, 2023, Keryx and Panion & BF Biotech, Inc., or Panion, filed a complaint for patent infringement against Zydus, Zydus Pharmaceuticals (USA) Inc., and Zydus Lifesciences Limited in the Delaware District Court arising from Zydus' ANDA filing with the FDA.

Stockholder Litigation Relating to the Merger

On June 28, 2018, we entered into an Agreement and Plan of Merger with 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.

On July 15, 2021, a purported former Keryx stockholder filed a putative class action in the Supreme Court of the State of New York against Akebia, a current officer of Akebia (John P. Butler), a former officer of Akebia (Jason A. Amello), former directors of Akebia (Muneer A. Satter, Scott A. Canute, Michael D. Clayman, Maxine Gowen, Duane Nash, Ronald C. Renaud, Jr., and Michael S. Wyzga), a current director of Akebia (Cynthia Smith), a former director and officer of Keryx (Jodie P. Morrison), a former officer of Keryx (Scott A. Holmes) and former directors of Keryx (Michael Rogers, Kevin J. Cameron, Steven C. Gilman, Daniel P. Regan, Mark J. Enyedy, and Michael T. Heffernan, some of whom are current members of our Board of Directors). The action is captioned Loper v. Akebia Therapeutics, Inc., et al., or the *Loper* Action. The complaint in the *Loper* Action alleges that the registration statement filed in connection with the Merger contained allegedly false and misleading statements or failed to disclose certain allegedly material information in violation of Section 11, 12(a)(2), and 15 of the Securities Act of 1933, as amended. It alleges, among other things, that Akebia failed to disclose heightened safety risks that allegedly threatened the prospects of the Phase 3 PRO2TECT clinical trial and the commercial viability of vadadustat. The complaint in the *Loper* Action seeks damages including interest thereon, an award of plaintiffs' and the class's costs and expenses, including counsel fees and expert fees, and rescission, disgorgement, or such other equitable or injunctive relief that the Court deems appropriate.

On August 16, 2021, another purported former Keryx stockholder filed a putative class action making substantially similar allegations and asserting the same claims as the *Loper* Action, also in the Supreme Court of the State of New York against Akebia and many of the same individual defendants named in the *Loper* Action. The action is captioned Panicho v. Akebia Therapeutics, Inc., et al., or the *Panicho* Action.

On September 13, 2021, the parties in the *Loper* Action and *Panicho* Action entered into a joint stipulation and proposed order, which provided for the consolidation of the two actions under the caption In re Akebia Therapeutics, Inc. Securities Litigation, or the Consolidated State Action. On October 27, 2021, plaintiffs filed a consolidated complaint in the Consolidated State Action. On January 10, 2022, defendants moved to dismiss the consolidated complaint in its entirety. Briefing on defendants' motion to dismiss was completed on April 22, 2022. Oral argument was held on October 7, 2022, and the Court dismissed the complaint without prejudice on October 17, 2022, giving plaintiffs thirty days to amend their complaint. On November 16, 2022, plaintiffs filed an amended consolidated complaint, asserting the same claims and seeking the same relief as the consolidated complaint. On January 18, 2023, defendants moved to dismiss the amended consolidated complaint in its entirety. Briefing on defendants' motion to dismiss the amended consolidated complaint was completed on April 5, 2023. Oral argument is currently scheduled to be held on June 21, 2023.

We deny any allegations of wrongdoing and intend to continue vigorously defending against the one active stockholder lawsuit described in this Legal Proceedings section, the Consolidated State Action. There is no assurance, however, that we will be successful in the defense of this action, or any associated appeals, or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of this action. Moreover, we are unable to predict the outcome or reasonably estimate a range of possible losses at this time. A resolution of the Consolidated State Action 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 the action is resolved.

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 condition, financial statements, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to our Financial Position, Need for Additional Capital and Growth Strategy

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 requires upfront capital expenditures and there is 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, commercializing Auryxia, and providing general and administrative support for these operations. We have financed our operations primarily through sales of equity securities, our strategic collaborations and product revenues, a royalty monetization transaction and debt. Prior to the merger, or the Merger, whereby Keryx Biopharmaceuticals, Inc., or Keryx, became our wholly owned subsidiary, 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 we have incurred net losses each year since our inception, including a net loss of $26.2 million for the three months ended March 31, 2023. As of March 31, 2023, we had an accumulated deficit of $1.6 billion. We cannot guarantee when, if ever, we will become profitable.

In March 2022, we received a complete response letter, or CRL, from the FDA regarding our NDA for vadadustat, our lead investigational product candidate, for the treatment of anemia associated with CKD. The FDA concluded that the data in the NDA do not support a favorable benefit-risk assessment of vadadustat for dialysis and non-dialysis patients. In October 2022, we submitted a Formal Dispute Resolution Request, or FDRR, to the FDA. The FDRR focuses on the favorable balance between the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult patients on dialysis in light of safety concerns expressed by the FDA in the CRL for dialysis patients related to the rate of adjudicated thromboembolic events driven by vascular access thrombosis for vadadustat compared to the active comparator and the risk of drug-induced liver injury. In February 2023, we received a second interim response from the FDA to our FDRR, and there can be no assurances that we will be successful in our appeal and obtain approval for vadadustat in a timely manner, on favorable terms, or at all. As a result, the regulatory approval process for vadadustat in the U.S. is highly uncertain. We may not obtain approval at all, and if we are able to obtain approval, the expense and time to do so could adversely impact our ability to successfully commercialize vadadustat or conduct our other business operations, and our financial condition could be materially harmed.

Our ability to generate product revenue and achieve profitability depends on the overall success of Auryxia(R), vadadustat, if approved, and any current or future product candidates, including those that may be in-licensed or acquired, which depends on several factors, including:

- obtaining adequate or favorable pricing and reimbursement from private and governmental payors for Auryxia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- obtaining and maintaining market acceptance of Auryxia, vadadustat, if approved, and any other product candidate, including those that may be in-licensed or acquired;
- 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, receives approval and obtaining adequate market share in those markets;
- addressing the issues identified in the CRL for vadadustat that we received from the FDA and the outcome of our appeal;
- the timing and scope of marketing approvals for vadadustat, if approved, and any other product candidate, if approved, including those that may be in-licensed or acquired; maintaining marketing approvals for Auryxia, vadadustat, if approved, and any other product, including those that may be in-licensed or acquired;
- actual or perceived advantages or disadvantages of our products or product candidates as compared to alternative treatments, including their respective safety, tolerability and efficacy profiles, the potential convenience and ease of administration and cost;
- maintaining an acceptable safety and tolerability profile of our approved products, including the frequency and severity of any side effects;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, based, in part, on their perception of our clinical trial data and/or the actual or perceived safety, tolerability and efficacy profile;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate supplies of products that are compliant with good manufacturing practices, or GMPs, to support the clinical development and the market demand for Auryxia, vadadustat, if approved, and any other product and product candidate, including those that may be in-licensed or acquired;
- current and future restrictions or limitations on our approved or future indications and patient populations or other adverse regulatory actions or in the event that the FDA requires Risk Evaluation and Mitigation Strategies, or REMS, or risk management plans that use restrictive risk minimization strategies;
- the effectiveness of our sales, marketing, manufacturing and distribution strategies and operations;

- competing effectively with any products for the same or similar indications as our products;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents and trade secrets; and
- the impact of the COVID-19 pandemic on the above factors, including the disproportionate impact of the COVID-19 pandemic on CKD patients, the adverse impact on the phosphate binder market in which we compete, and the limitation of our sales professionals to meet in person with healthcare professionals as the result of limitations on access for non-patients.

Our ability to achieve profitability also depends on our ability to manage our expenses. Following receipt of the CRL, in April and May 2022, we implemented a reduction of our workforce, by approximately 42% across all areas of the Company (47% inclusive of the closing of the majority of open positions), including several members of management. In November 2022, we also implemented a reduction of our workforce, by approximately 14% consisting of individuals within our commercial organization as a result of our decision to shift to a strategic account management focused model for our commercial efforts. We recorded a restructuring charge of approximately $15.9 million and $0.1 million in the year ended December 31, 2022 and the three months ended March 31, 2023, respectively, primarily related to contractual termination benefits including severance, non-cash stock-based compensation expense, healthcare and related benefits. However, we may incur additional costs not currently contemplated due to events associated with or resulting from the workforce reductions. Additionally, the reductions in workforce could impact our operations, including our commercialization of Auryxia, which could affect our ability to generate revenue.

We expect to continue to incur additional operating expenses, including additional research and development expenses to our pipeline, additional costs related to vadadustat, and research and development and selling, general and administrative expenses for ongoing development and commercialization of Auryxia, which could lead to operating losses for the foreseeable future. In addition to any additional costs not currently contemplated due to events associated with or resulting from the workforce reductions noted above, our ability to achieve profitability and our financial position will depend, in part, on the rate of our future expenditures, on product revenue, collaboration revenue, and our ability to obtain additional funding. On June 30, 2022, we entered into a Termination and Settlement Agreement, or the Termination Agreement, with Otsuka Pharmaceutical Co. Ltd., or Otsuka, pursuant to which we agreed to the immediate termination of the December 18, 2016 collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement, and the April 25, 2017 collaboration and license agreement with Otsuka, or the Otsuka International Agreement, in exchange for the payment of $55.0 million to us and the agreement between the parties with respect to the conduct of certain activities. Unless and until we are able to find a new partner for vadadustat in Europe and other countries previously licensed to Otsuka, we will incur additional expenses in connection with the development of vadadustat and will receive less collaboration revenue and, if approved, product revenue than originally anticipated. In addition, we expect to continue to incur significant expenses if and as we:

- continue our commercialization activities for Auryxia and vadadustat, if we are able to obtain marketing approval for vadadustat following receipt of the CRL from the FDA in March 2022, and any other product or product candidate, including those that may be in-licensed or acquired;
- address the issues identified in the CRL for vadadustat that we received from the FDA and pursue our appeal of the CRL for vadadustat with the FDA;
- conduct and enroll patients in any clinical trials, including post-marketing studies or any other clinical trials for Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired;
- seek marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired;
- maintain marketing approvals for Auryxia and vadadustat, if we are able to obtain marketing approval for vadadustat following receipt of the CRL from the FDA in March 2022, and any other product, including those that may be in-licensed or acquired;
- manufacture Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, for commercial sale and clinical trials;
- conduct discovery and development activities for additional product candidates or platforms that may lead to the discovery of 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 and commercialize other product candidates and technologies;
- continue to repay, and pay any associated pre-payment penalties, if applicable, the senior secured term loans in an aggregate principal amount of $51.0 million as of March 31, 2023, or the Term Loans, that were made available to us pursuant to the Loan Agreement;
- make royalty, milestone or other payments under our license agreements and any future license agreements;
- maintain, protect and expand our intellectual property portfolio;
- make decisions with respect to our personnel, including the retention of key employees;
- make decisions with respect to our infrastructure, including to support our operations as a fully integrated, publicly traded biopharmaceutical company; and

- experience any additional delays or encounter issues with any of the above.

We have and will continue to expend significant resources on our legal proceedings, as described below under Part II, Item 1. Legal Proceedings, or any other legal proceedings brought by or 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.

We will continue to incur substantial expenditures relating to continued commercialization and post-marketing requirements for Auryxia and vadadustat, if we are able to obtain marketing approval for vadadustat following receipt of the CRL from the FDA in March 2022, and any other products, including those that may be in-licensed or acquired, as well as costs relating to the research and development of any other product candidate, including those that may be in-licensed or acquired. 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 FDA, the European Medicines Agency, or the 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 conduct any additional clinical trials, whether in order to obtain approval or as a post-approval study, including any additional clinical trial that we decide to conduct for vadadustat, to perform studies in addition to, different from or larger than those currently planned, if there are any delays in completing our clinical trials or if there are further delays in or issues with obtaining marketing approval for vadadustat in the United States or other jurisdictions. 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 sought or the patient population for treatment is narrowed by competition, physician choice, coverage or reimbursement, or payor or treatment guidelines. Even though we generate product revenue from Auryxia and royalties from Riona™ and Vafseo™ in Japan and may generate revenue and royalties from the sale of any products that may be approved in the future, including those that may be in-licensed or acquired, we may never generate revenue and royalties that are significant enough for us to become and remain profitable, and we will need to obtain additional funding to continue to fund our operating plan beyond Auryxia and certain development activities, and achieve strategic growth.

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

As of March 31, 2023, our cash and cash equivalents were $57.0 million. We expect to continue to expend substantial amounts of cash for the foreseeable future as we continue to commercialize Auryxia; pursue our appeal for vadadustat in the U.S. with the FDA; support the regulatory process with respect to vadadustat with the ACCESS Consortium; and develop and commercialize any other product or product candidate, including those that may be in-licensed or acquired. These expenditures will include costs associated with research and development, manufacturing, potentially obtaining marketing approvals and marketing products approved for sale. In addition, other unanticipated costs may arise. Because the outcomes of our current and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of funding necessary to successfully complete clinical development for any current or future product candidates, including vadadustat depending on what is required to address the issues identified in the CRL for vadadustat, including the outcome of our appeal and if additional clinical trials are required in order to obtain marketing approval, or to complete post-marketing studies for Auryxia and vadadustat, if approved. Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of conducting clinical trials or any post-marketing requirements or any other clinical trials for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired;
- the cost and timing of commercialization activities, including product manufacturing, marketing, sales and distribution costs, for Auryxia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- the results of our meetings with the FDA, the EMA and other regulatory authorities and any consequential effects, including on timing of and ability to obtain and maintain marketing approval, study design, study size and resulting operating costs;
- any difficulties or delays in conducting our clinical trials, or enrolling patients in our clinical trials, for Auryxia, vadadustat or any other product candidates;

- the outcome of our efforts to obtain marketing approval for vadadustat in the United States and in other jurisdictions and any other product candidates, including those that may be in-licensed or acquired, including any additional clinical trials or post-approval commitments imposed by regulatory authorities;
- the timing of, and the costs involved in obtaining, marketing approvals for vadadustat, including in the United States and certain other markets, and any other product candidate, including those that may be in-licensed or acquired, including to fund the preparation, filing and prosecution of regulatory submissions;
- the costs of maintaining marketing approvals for Auryxia or any other product, including those that may be in-licensed or acquired;
- the number of generic versions of Auryxia that enter the market following loss of exclusivity for Auryxia in March 2025, and the timing of, and the magnitude of, the impact on the price of Auryxia;
- the cost of securing and validating commercial manufacturing for any of our product candidates, including those that may be in-licensed or acquired, and maintaining our manufacturing arrangements for Auryxia and vadadustat or any other product, including those that may be in-licensed or acquired, 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;
- our status as a publicly traded company on the Nasdaq Capital Market;
- our decisions with respect to personnel;
- our decisions with respect to infrastructure; and
- the extent to which we engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we could develop and market commercial products, or develop other product candidates and technologies.

We will need to obtain substantial additional funding to fund our operating plan beyond Auryxia and certain development activities, and achieve strategic growth. 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 to fund our current operating plan through at least the next twelve months from the filing of this Quarterly Report on Form 10-Q. However, if our operating performance deteriorates significantly from the levels expected in our operating plan, it could have an effect on our liquidity and our ability to continue as a going concern in the future. 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 numerous risks and uncertainties, and actual results could vary as a result of a number of factors, many of which are outside our control. 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. In addition, if we fail to satisfy any of the covenants under our Loan Agreement with Pharmakon, including the covenant that our Annual Report on Form 10-K for the fiscal year ending December 31, 2023 not be qualified as to going concern, and the loan is accelerated, we may not have sufficient resources to fund our operating plan through the next twelve months. There can be no assurance that the current operating plan will be achieved in the time frame anticipated by us, or that our cash resources will fund our operating plan for the period anticipated by us, or that additional funding will be available on terms acceptable to us, 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 and any other products or product candidates, including those that may be in-licensed or acquired, or to continue to seek regulatory approval for vadadustat. 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 and/or commercialization of Auryxia and any other products or product candidates, including those that may be in-licensed or acquired, or to take any actions with respect to vadadustat depending on future decisions with respect to vadadustat in the U.S. 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 future cash needs through product revenue, potential strategic transactions, public or private equity or debt 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. Additional 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, we may have to relinquish valuable rights to our portfolio and future revenue streams, and enter into agreements that would restrict our operations and strategic flexibility. 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 when needed, we may not be able to pursue planned development and commercialization activities and we may need to grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

If we fail to regain compliance with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

On May 12, 2022, we received a deficiency letter from the Listing Qualifications Department of the Nasdaq Stock Market, or Nasdaq, notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the minimum $1.00 per share requirement for continued inclusion on the Nasdaq Global Market, referred to as the minimum bid price rule. In accordance with Nasdaq Listing Rules, we were provided an initial period of 180 calendar days, or until November 8, 2022, to regain compliance with the minimum bid price rule. We did not regain compliance with the minimum bid price rule by the initial compliance date.

On November 9, 2022, Nasdaq notified us that we were eligible for an additional 180 calendar day period, or until May 8, 2023, to regain compliance with the minimum bid price rule. Nasdaq's determination was based on our meeting the continued listing requirement for market value of publicly held shares and all other applicable requirements for initial listing on the Nasdaq Capital Market with the exception of bid price requirement, and our written notice of our intention to cure the deficiency during the second compliance period by effecting a reverse stock split, if necessary. On November 9, 2022, Nasdaq approved our transfer from the Nasdaq Global Market to the Nasdaq Capital Market, a continuous trading market that operates in substantially the same manner as the Nasdaq Global Market. The transfer became effective at the opening of business on November 11, 2022.

We held a special meeting of stockholders on May 4, 2023, at which meeting our stockholders did not approve the reverse stock split that our Board had recommended, the primary intent of which was to increase the price of our common stock to meet the price criteria for continued listing on Nasdaq.

To date, we have not regained compliance with the minimum bid price rule, and we do not expect to regain compliance during the additional compliance period. If we do not regain compliance with the minimum bid price rule by the required date and we are not eligible for any additional compliance period at that time, the Nasdaq Listing Qualifications Department staff will provide us written notification that our common stock may be delisted. At that time, we plan to appeal the staff's delisting determination to a Nasdaq Listing Qualifications Panel. We expect that our common stock would remain listed pending the panel's decision. However, there can be no assurance that, even if we appeal the staff's delisting determination to the Nasdaq Listing Qualifications Panel, such appeal would be successful. In addition, even if our appeal is successful, we will still need to regain compliance with the minimum bid price rule during the additional compliance period granted by the Nasdaq Listing Qualifications Panel, and there can be no assurance that we will be able to regain compliance with the minimum bid price rule during that time.

There are many factors that may adversely affect our minimum bid price, including those described throughout this section titled "Risk Factors." Many of these factors are outside of our control. As a result, we may not be able to sustain compliance with the minimum bid price rule in the long term. Any potential delisting of our common stock from the Nasdaq Capital Market would likely result in decreased liquidity and increased volatility for our common stock and would adversely affect our ability to raise additional capital or to enter into strategic transactions. Any potential delisting of our common stock from the Nasdaq Capital Market would also make it more difficult for our stockholders to sell our common stock in the public market.

We may not be successful in our efforts to identify, acquire, in-license, discover, develop and commercialize additional products or product candidates or our decisions to prioritize the development of certain product candidates over others may not be successful, which could impair our ability to grow.

Although we continue to focus a substantial amount of our efforts on the commercialization of Auryxia and to pursue our appeal for vadadustat in the U.S. with the FDA and to seek regulatory approval for vadadustat in other territories, a key element of our long-term growth strategy is to develop additional product candidates and acquire, in-license, 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 other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and/or achieve market acceptance;
- a product candidate we develop and seek regulatory approval for, including vadadustat, may not be approved by the FDA on a timely basis, or at all;
- 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 commercially 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 occur, we may be forced to abandon our research and 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 may have a material adverse effect on our business.

Because we have limited financial and managerial resources, especially as a result of the CRL for vadadustat that we received in March 2022 and the reductions in workforce that we implemented in 2022, 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, or out license rights to product candidates, that later prove to have greater commercial potential. For example, as a result of receipt of the CRL and implementation of the reductions in workforce, we delayed certain research activities. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities on a timely basis, or at all. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

Because our internal research capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists and institutions, and other researchers to sell or license product candidates, 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 identifying, selecting, 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. 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, the Japanese Pharmaceuticals and Medical Devices Agency, or 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 of our products will be manufactured in a cost effective manner, 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, acquire, in-license or develop suitable additional products or product candidates, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential products, product candidates or other programs that ultimately prove to be unsuccessful.

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 merger, acquisition or in-license of assets, businesses, or rights to products, product candidates or technologies or through strategic alliances or collaborations, similar to the Merger and our existing and prior collaboration and license arrangements. We may not identify suitable strategic transactions, or complete such transactions in a timely manner, on favorable terms, 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 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 and integration 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. For example, on June 4, 2021, we entered into a license agreement, the Cyclerion Agreement, with Cyclerion Therapeutics Inc., or Cyclerion, pursuant to which Cyclerion granted us an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase, or sGC, stimulator. Although we have progressed preclinical studies for praliciguat, we need to do additional work to manufacture product for clinical trials before we can initiate the trials, and when started, we may be unsuccessful in developing praliciguat. If any of the assumptions that we made in valuing the transaction, including the costs or timing of development of, or the potential benefits of, praliciguat, were incorrect, we may not recognize the anticipated benefits of the transaction and our business could be harmed.

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

- incurring substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- exposure to known and unknown liabilities, including contingent liabilities, possible intellectual property infringement claims, violations of laws, tax liabilities and commercial disputes;
- higher than expected acquisition and integration costs;
- difficulty in integrating operations, processes, systems and personnel of any acquired business;
- increased amortization expenses or, in the case of a write-down of the value of acquired assets, impairment losses, such as the Auryxia intangible asset impairment in the second quarter of 2020 and corresponding adjustments to the estimated useful life of the developed product rights for Auryxia;
- 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 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.

Our business has been and may continue to be, directly or indirectly, adversely affected by the COVID-19 pandemic.

The COVID-19 pandemic has presented a substantial public health and economic challenge around the world and has affected, and may continue to affect, our business, patients, healthcare providers with whom we interact, customers, our contract manufacturing organizations, or CMOs, and other vendors. The full extent to which the COVID-19 pandemic and the lasting effects of the pandemic will directly or indirectly impact our business, results of operations and financial condition continues to depend on future developments that are highly uncertain and cannot be accurately predicted, including any resurgences or variants of COVID-19, the actions taken to contain it or treat its impact and the economic and other impacts on local, regional, national and international markets where the healthcare providers with whom we interact, our CMOs, and our other vendors operate. On January 30, 2023, the Biden Administration announced that it will end the public health emergency declarations related to COVID-19 on May 11, 2023. On January 31, 2023, the FDA indicated that it would issue a Federal Register notice describing how the termination of the public health emergency will impact the agency's COVID-19 related guidance. Thereafter, on March 13, 2023, the FDA announced that it will end twenty-two COVID-19-related policies when the public health emergency ends on May 11, 2023 and allow twenty-two to continue for 180 days. The FDA plans to retain twenty-four COVID-19-related policies with appropriate changes and four whose duration is not tied to the end of the public health emergency. At this point, it is unclear how, if at all, these developments will impact our efforts to develop and commercialize our product candidates.

We believe our revenue growth was negatively impacted by the COVID-19 pandemic in 2021, 2022 and the first quarter of 2023 primarily as the CKD patient populations that we serve experienced both high hospitalization and mortality rates due to COVID-19, and the pandemic had an adverse impact on the phosphate binder market in which Auryxia competes. Labor shortages and costs have adversely impacted dialysis providers. These impacts have refocused clinical efforts in addressing bone and mineral disorders like hyperphosphatemia to more acute operational issues to ensure patients receive dialysis treatments and still some patients have been rescheduled or missed treatments due to labor shortages. We believe, this and potentially other factors, has led to the reduction in the phosphate binder market, which has not experienced growth since early 2020. While we are unable to quantify the impact of the COVID-19 pandemic on future revenues and revenue growth, the

COVID-19 pandemic and the ongoing impacts from the COVID-19 pandemic continue to adversely and disproportionately impact CKD patients and the phosphate binder market; therefore, we expect the ongoing impacts from the pandemic to continue to have a negative impact on our revenue growth for the foreseeable future.

In addition, several healthcare facilities have previously restricted access for non-patients, including the members of our sales force. For example, DaVita, Inc., or DaVita, and Fresenius Medical Care, or Fresenius, which account for a vast majority of the dialysis population in the United States, have previously restricted access to their clinics. As a result, we continue to engage with some healthcare providers and other customers virtually, where possible. The restrictions on our customer-facing employees' in-person interactions with healthcare providers have, and could continue to, negatively impact our access to healthcare providers and, ultimately, our sales, including with respect to vadadustat, if approved. Recently, such precautionary measures have been relaxed at certain healthcare facilities and, as a result, members of our sales force have resumed in person interactions with certain customers. Nevertheless, some restrictions remain, and more restrictions may be put in place again due to a resurgence in COVID-19 cases, including those involving new variants of COVID-19, which may be more contagious and more severe than prior strains of the virus. Given this uncertain environment and the disproportionate impact of the COVID-19 pandemic on CKD patients, we are actively monitoring the demand in the United States for Auryxia and will be for vadadustat, if approved, including the potential for further declines or changes in prescription trends and customer orders, which could have a material adverse effect on our business, results of operations, and financial condition.

In addition, the direct and indirect impacts of the pandemic or the response efforts to the pandemic, including, among others, competition for labor and resources and increases in labor, sourcing, manufacturing and shipping costs, may cause disruptions to, closures of or other impacts on our CMOs and other vendors in our supply chain on which we rely for the supply of our products and product candidates. For example, areas of China have recently continued to implement lockdowns for COVID-19, which could impact the global supply chain. At this time, our CMOs continue to operate at or near normal levels. However, it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our contract manufacturers' ability to manufacture and deliver Auryxia and vadadustat (if approved in the United States or EMA and which is currently marketed under the trade name Vafseo™ by MTPC in Japan), which may result in increased costs and delays, or disruptions to the manufacturing and supply of our products. These impacts could have a negative effect on our inventory reserves, which could result in an increase in inventory write-offs due to expiry.

If we or any of the third parties with whom we engage, including our collaboration partners, vendors, or any of our customers were to experience further shutdowns, delays or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned, and our revenue expectations, could be materially and negatively impacted, which could have a material adverse effect on our business and our financial results.

While we are working to mitigate the impacts on our business, we are mindful that many of these risks and the impact to the larger healthcare market are outside of our control. The COVID-19 pandemic has, and may continue to, significantly impact the phosphate binder market in which we compete and economies and financial markets worldwide, which could result in adverse effects on our business and operations, impact our ability to raise additional funds and impact the volatility of our stock price and trading in our stock. Even after the COVID-19 pandemic has been contained or mitigated, we may continue to experience adverse impacts to our business as a result of the adverse impact on the patient population for Auryxia, the decline in the phosphate binder market and any economic recession or depression that has occurred or may occur in the future.

Risks Related to our Financial Arrangements

Our obligations in connection with the loan agreement with Pharmakon and requirements and restrictions in the loan agreement could adversely affect our financial condition and restrict our operations.

We entered into the Loan Agreement with Pharmakon, pursuant to which the Term Loans were made available to us in two tranches. The first tranche of $80.0 million closed on November 25, 2019, and the second tranche of $20.0 million closed on December 10, 2020. See Note 10 to our condensed consolidated financial statements in Part I, Item 1. Financial Statements of this Quarterly Report on Form 10-Q for additional information regarding our obligations under the Loan Agreement.

The Loan Agreement contains affirmative and negative covenants applicable to us and our subsidiaries, including maintaining, on an annual basis, a minimum liquidity threshold and, on a quarterly basis, a minimum net sales threshold for Auryxia. In addition, the Loan Agreement contains covenants that our Annual Reports on Form 10-K, must not be subject to any qualification as to going concern. Failure to maintain compliance with these or other covenants would result in an event of default under the Loan Agreement, which could result in enforcement action, including acceleration of amounts due under the Loan Agreement. Additionally, the liabilities under the Loan Agreement will be accelerated, subject to certain exceptions, if we are required to repay to CSL Vifor all or more than a specified amount of the working capital facility established in connection with the Second Amended and Restated License Agreement that we entered into with CSL Vifor, in February 2022, or the Vifor Second Amended Agreement, as a result of certain terminations of the Vifor Second Amended Agreement or due to a reduction in the balance of the working capital facility by more than a prespecified amount.

In the event there is an acceleration of our and certain of our subsidiaries' liabilities under the Loan Agreement as a result of an event of default or otherwise, we may not have sufficient funds or may be unable to arrange for additional financing to repay the liabilities or to make any accelerated payments, and Pharmakon could seek to enforce security interests in the collateral securing the Loan Agreement and our guarantee of the Term Loans, which would have a material adverse effect on our business, financial condition and results of operations.

The Loan Agreement permits voluntary prepayment at any time in whole or in part, subject to prepayment premiums and make-whole premiums prior to certain dates. We made a voluntary prepayment of $25.0 million, including $0.5 million of prepayment penalties on July 15, 2022, pursuant to the Second Amendment and Waiver. This represented the repayment of $5.0 million of the first tranche and the full $20.0 million of the second tranche. Upon a change of control, mandatory prepayment provisions require us to prepay the principal amount outstanding, the applicable prepayment premium and make-whole premium and accrued and unpaid interest. In addition, our obligations in connection with the Loan Agreement could have additional significant adverse consequences, including, among other things:

- restricting our activities, including limitations on transferring certain of our assets, engaging in certain transactions, terminating certain agreements, including the Vifor Second Amended Agreement, incurring certain additional indebtedness, creating certain liens, paying dividends or making certain other distributions and investments;
- limiting our flexibility in planning for, or reacting to, changes in our business and our industry;
- placing us at a possible competitive disadvantage compared to our competitors who have a smaller amount of debt or competitors with comparable debt at more favorable interest rates; and
- limiting our ability to borrow additional amounts for working capital, capital expenditures, research and development efforts, acquisitions, debt service requirements, execution of our business strategy and other purposes.

Any of these factors could materially and adversely affect our business, financial condition and results of operations.

Our Royalty Interest Acquisition Agreement with HealthCare Royalty Partners IV, L.P. contains various covenants and other provisions, which, if violated, could materially adversely affect our financial condition.

On February 25, 2021, we entered into a royalty interest acquisition agreement, or the Royalty Agreement, with HealthCare Royalty Partners IV, L.P., or HCR, pursuant to which we sold to HCR our right to the to receive royalties and sales milestones for vadadustat, collectively the Royalty Interest Payments, in each case, payable to us under our Collaboration Agreement dated December 11, 2015, or the MTPC Agreement, with Mitsubishi Tanabe Pharma Corporation, or MTPC, subject to an annual maximum "cap" of $13.0 million, or the Annual Cap, and an aggregate maximum "cap" of $150.0 million, or the Aggregate Cap. Under the Royalty Agreement, we are required to comply with various covenants, including obligations to take certain actions, such as actions with respect to the Royalty Interest Payments, the MTPC Agreement, our agreement with MTPC for the commercial supply of vadadustat drug product, and our intellectual property. In addition, the Royalty Agreement includes customary events of default upon the occurrence of enumerated events, including failure to perform certain covenants and the occurrence of insolvency events. In the event we violate certain covenants and other provisions, we may not receive sales milestones from HCR even if the applicable sales thresholds are met. Upon the occurrence of an event of default, HCR would have the ability to exercise all available remedies in law and equity, which could have a material adverse effect on our financial condition.

Risks Related to Commercialization

Our business is substantially dependent on the commercial success of Auryxia. If we are unable to continue to successfully commercialize Auryxia, our results or operations and financial condition will be materially harmed.

Our business and our ability to generate product revenue largely depend on our, and our collaborators', ability to successfully commercialize Auryxia. Our ability to generate revenue depends on our ability to execute on our commercialization plans, and the size of the market for, and the level of market acceptance of, Auryxia and any other product or product candidate, including those that may be in-licensed or acquired. If the size of any market for which a product or product candidate is approved decreases or is smaller than we anticipate, our revenue and results of operations could be materially adversely affected. For example, the phosphate binder market has declined since 2020, which we believe was partially a result of the COVID-19 pandemic. If the phosphate market does not recover or continues to decline, our revenue from Auryxia could be materially adversely affected.

Market acceptance is also critical to our ability to generate significant product revenue. Any product may achieve only limited market acceptance or none at all. If Auryxia, or any of our product candidates that is approved, is not accepted by the market to the extent that we expect or market acceptance decreases, we may not be able to generate significant product revenue and our

business would be materially harmed. Market acceptance of Auryxia or any other approved product depends on a number of factors, including:

- the availability of adequate coverage and reimbursement by and the availability of discounts, rebates and price concessions from third party payors, pharmacy benefit managers, or PBMs, and governmental authorities;
- the safety and efficacy of the product, as demonstrated in clinical trials and in the post-marketing setting;
- the prevalence and complications of the disease treated by the 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 the product;
- 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 frequency and severity of adverse side effects;
- favorable or 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 the product together with other medications, if any.

If we are unable to maintain or expand, or, if vadadustat is approved, initiate, sales and marketing capabilities or enter into additional agreements with third parties, we may not be successful in commercializing Auryxia, vadadustat, if approved, or any other product candidates that may be approved.

In order to market Auryxia and any other approved product, we intend to continue to invest in sales and marketing, which will require substantial effort and significant management and financial resources. We have built a commercial infrastructure and sales force in the United States for Auryxia, our only commercial product. However, following receipt of the CRL, in April and May 2022, we implemented a reduction of our workforce by approximately 42% across all areas of the Company (47% inclusive of the closing of the majority of open positions), including several members of our sales and marketing team and management. In November 2022, we also implemented a reduction of our workforce, by approximately 14% consisting of individuals within our commercial organization as a result of our decision to shift to a strategic account management focused model for our commercial efforts. If the remaining sales and marketing team cannot successfully commercialize Auryxia, or if additional sales and marketing employees decide to leave as a result of the reduction in workforce or otherwise, it could have a material adverse effect on Auryxia revenue and our financial condition.

If we obtain regulatory approval to market vadadustat in the U.S., we believe that we can leverage the current commercial foundation for vadadustat in the U.S., but if we are unable to do so successfully this would materially harm our business. Additionally, training a sales force to successfully sell and market a new commercial product is expensive and time-consuming and could delay any commercial launch of such product candidate or distract the sales force from promoting Auryxia. We may underestimate the size of the sales force required for a successful product launch and we may need to expand our sales force earlier and at a higher cost than we anticipated. In 2021 and early 2022, we incurred commercialization expenses for vadadustat that were premature or unnecessary as a result of the receipt of the CRL for vadadustat, and may in the future incur additional commercialization expenses prematurely or unnecessarily if we do not receive marketing approval in the timeframe we expect, or at all.

We 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 and retaining qualified personnel with experience in our industry is difficult. Further, our reductions in workforce may further exacerbate these conditions and interfere with our ability to find and retain qualified personnel. As a result, we may not be able to retain our existing employees or hire new employees quickly enough to meet our needs. At the same time, we may face high turnover, requiring us to expend time and resources to source, train and integrate new employees.

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

- potential inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;

- 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, especially as a result of the receipt of the CRL for vadadustat; and
- costs and expenses associated with maintaining our own sales and marketing organization.

If we are unable to maintain our own sales and marketing capabilities, we will not be successful in commercializing Auryxia, vadadustat, if approved, and any other product candidate that may be approved.

Furthermore, if we are unable to maintain our arrangements with third parties with respect to sales and marketing, if we are unsuccessful in entering into additional arrangements with third parties to sell and market our products or we are unable to do so on terms that are favorable to us, or if such third parties are unable to carry out their obligations under such arrangements, it will be difficult to successfully commercialize our product and product candidates, including vadadustat, if approved. For example, if in connection with the Vifor Second Amended Agreement, we experience difficulties with CSL Vifor, or if CSL Vifor experiences difficulties with other parties to whom it expects to sell vadadustat, if approved, our ability to commercialize vadadustat, if approved, will be severely hindered and our business operations will be materially harmed.

Our, or our partners', failure to obtain or maintain adequate coverage, pricing and reimbursement for Auryxia, vadadustat, if approved, or any other future approved products, could have a material adverse effect on our or our collaboration partners' ability to sell such approved products profitably and otherwise have a material adverse impact on our business.

Market acceptance and sales of any approved products, including Auryxia and, if approved, vadadustat, depends significantly on the availability of adequate coverage and reimbursement from third party payors and may be affected by existing and future healthcare reform measures. Governmental authorities, third party payors, and PBMs decide which drugs they will cover, as well as establish formularies or implement other mechanisms to manage utilization of products and determine reimbursement levels. We cannot be sure that coverage or adequate reimbursement will be available for Auryxia, vadadustat, if approved, or any of our potential future products. Even if we obtain coverage for an 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 product. If reimbursement is not available or is limited, we may not be able to commercialize certain of our products. Coverage and reimbursement by a governmental authority, third-party payor or PBM may depend upon a number of factors, including the determination that use of a product is:

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

Obtaining coverage and reimbursement approval for a product from a governmental authority, PBM or a 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 governmental authorities, PBMs and third-party payors with varying coverage and reimbursement levels for pharmaceutical products, and the timing of commencement of reimbursement by a governmental payor can be dependent on the assignment of codes via the Healthcare Common Procedural Coding System, which codes are assigned on a quarterly basis. Within Medicare, for oral drugs dispensed by pharmacies and also administered in facilities, coverage and reimbursement may vary depending on the setting. CMS, local Medicare administrative contractors, Medicare Part D plans and/or PBMs operating on behalf of 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 under Part D. However, in September 2018, CMS decided that Auryxia would no longer be covered by Medicare for the treatment of iron deficiency anemia, or IDA, in adult patients with NDD-CKD, or the CMS Decision. While this decision does not impact CMS coverage for the control of serum phosphorus levels in adult patients with DD-CKD, or the Hyperphosphatemia Indication, it requires Part D plan sponsors to impose prior authorization or other steps to ensure that Auryxia is reimbursed only for the Hyperphosphatemia Indication. While we believe that the vast majority of the Medicare prescriptions written for Auryxia today are for the Hyperphosphatemia Indication and therefore will continue to be covered by Medicare with prior authorization, the CMS Decision has had and will continue to have an adverse impact on the sales and future growth of Auryxia for the Hyperphosphatemia Indication and the IDA Indication. For example, in the second quarter of 2020, we reduced our short-term and long-term Auryxia revenue forecast, primarily driven by the compounding impact of the CMS Decision. As a result, we recorded an impairment charge of $115.5 million to the Auryxia intangible asset associated with the developed product rights for Auryxia during the three months ended June 30, 2020.

Medicaid reimbursement of drugs varies by state. Private third-party payor reimbursement policies 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 and/or PBMs offering rebates or discounts on our products in order to obtain favorable formulary status and we may not be able to agree upon commercially reasonable terms with such third party payors or PBMs, 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. In addition, third party payors, PBMs and other entities that purchase our products may impose restrictions on our ability to raise prices for our products over time without incurring additional costs. Four distributors, Fresenius Medical Care Rx, McKesson Corporation, Cardinal Health, Inc. and Amerisource Bergen Drug Corporation, in the aggregate, accounted for a significant percentage of our gross revenue during the three months ended March 31, 2023. If we are not able to maintain our arrangements with these key distributors on favorable terms, on a timely basis or at all, or if there is any adverse change in one or more of these distributors' business practices or financial condition, it would adversely impact the market opportunity for Auryxia, our product revenues and operating results.

Furthermore, vadadustat was approved in Japan for the treatment of adult patients with anemia due to CKD and is being marketed by MTPC in Japan under the trade name Vafseo™. Pricing and reimbursement strategy is a key component of MTPC's commercialization plans for Vafseo in Japan. If coverage and reimbursement terms change, MTPC may not be able to, or may decide not to, continue commercialization of Vafseo in Japan.

We currently believe it is likely that vadadustat, if approved, will be reimbursed using the Transitional Drug Add-on Payment Adjustment, or TDAPA, followed by inclusion in the bundled reimbursement model for Medicare beneficiaries. For those that obtain dialysis through commercial insurance during the 30-month coordination period or through Medicaid prior to Medicare becoming primary payer after 90 days, patients may 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, applying for and obtaining reimbursement under the TDAPA is expected to take at least six months following approval, which will affect adoption, uptake and product revenue for vadadustat during that time, and if there are updates to the TDAPA rule that decrease the basis for reimbursement or eligibility criteria during the transition period or if the TDAPA is eliminated, then our profitability may be adversely affected. For example, the Medicare Payment Advisory Commission, or MedPAC, an independent legislative branch advisory body to Congress on issues related to the Medicare program, has recommended that TDAPA not be provided to newly approved drug products considered to fall within "functional categories" for which costs are already accounted for in the bundled reimbursement model, such as for anemia management drugs.

Further, if vadadustat is approved in the United States 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 providers, instead of through distributors, which we believe could be challenging. The dialysis market is unique and is dominated by two providers: DaVita and Fresenius, which account for a vast majority of the dialysis population in the United States. Under the Vifor Second Amended Agreement, we granted CSL Vifor an exclusive license to sell vadadustat to Fresenius Medical Care North America and its affiliates, including Fresenius Kidney Care Group LLC, to certain third-party dialysis organizations approved by us, to independent dialysis organizations that are members of group purchase organizations, and to certain non-retail specialty pharmacies in the United States. We refer to Fresenius Medical Care North America and its affiliates, these organizations and specialty pharmacies collectively as the "Supply Group". See Note 4 to our consolidated financial statements in Part I, Item 1. Financial Statements of this Quarterly Report on Form 10-Q for additional information regarding the Vifor Second Amended Agreement. If vadadustat is approved and we are not able to maintain the Vifor Second Amended Agreement or enter into a supply agreement with DaVita or other dialysis clinics, our business may be materially harmed.

Similar to how payor coverage may affect the sales of a product, formulary status within dialysis organizations may affect what products are prescribed within that specific organization. Therefore, if a product is not on a formulary, the prescribers within that organization may be less likely to prescribe that product or may have a difficult time prescribing that product, resulting in less sales. Further, one dialysis organization's determination to add a product to their formulary does not assure that other dialysis organizations will also add the product to theirs. There is always a risk a dialysis organization will not contract with a drug manufacturer for a specific product, resulting in that product not being on that organization's formulary. If any dialysis organization does not add vadadustat, if approved, to the formulary, our business may be materially harmed.

In addition, we may be unable to sell Auryxia or 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 re-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 are central to patient and provider acceptance of any products for which we receive marketing approval.

Further, in many countries outside the United States, a drug 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 EMA or another regulatory authority does not ensure approval by reimbursement authorities in that jurisdiction, and approval by one reimbursement authority outside the United States does not ensure approval by any other reimbursement authorities. However, the failure to obtain reimbursement in one jurisdiction may negatively impact our ability to obtain reimbursement in another jurisdiction. We may not be able to obtain such reimbursement approvals on a timely basis, if at all, and favorable pricing in certain countries depends on a number of factors, some of which are outside of our control. In addition, if vadadustat is approved outside of the United States, we plan to rely on a partner to obtain approval by reimbursement authorities outside the United States. If we are unsuccessful or delayed in entering into an agreement with a new partner, the launch of vadadustat following approval outside the United States may be delayed, which could have an adverse effect on our results of operations.

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 Auryxia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired. Our objective is to continue to commercialize Auryxia and develop and commercialize new products with clinically proven 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 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. Most of the phosphate binders listed above are now also available in generic forms. In addition, other agents are in development, including OPKO Health Inc.'s Alpharen™ Tablets (fermagate tablets) and Unicycive's Renazorb (lanthanum dioxycarbonate) or could otherwise enter the market, including Ardelyx, Inc.'s tenapanor (which is approved in the United States for the treatment of adults with irritable bowel syndrome with constipation, and for which Ardelyx resubmitted a new drug application to the FDA in April 2023 with respect to the control of serum phosphorus in adult patients with CKD on dialysis), 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 intravenous 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 for the treatment of IDA may impact the market for Auryxia, such as Shield Therapeutics plc's Feraccru® (ferric maltol), which is available in Europe for the treatment of IDA and Accrufer® (ferric maltol), which was launched in the United States for the treatment of IDA in July 2021.

Furthermore, Auryxia's commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective, safer or offer greater patient convenience than Auryxia. Other companies have product candidates in various stages of preclinical or clinical development to treat diseases and complications of the diseases for which we are marketing Auryxia. In addition, we and Keryx's licensors, Panion & BF Biotech, Inc., or Panion, and, as applicable, Dr. Hsu, entered into settlement agreements with all but one of the third parties who submitted Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the FDA, pursuant to which we granted licenses to market a generic version of Auryxia in the United States beginning in March 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature, which may impact our business and results of operation.

Drugs that may compete with vadadustat 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 CSL Vifor in the United States and Roche Holding Ltd. outside of the United States. Further, in February 2023 the FDA approved daprodustat, an oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor to be marketed as Jesduvroq by GlaxoSmithKline plc, or GSK, in the United States, as a once-a-day treatment of anemia due to CKD in adult patients who have been receiving dialysis for at least four months.

We and our partners may also face competition from potential new anemia therapies. There are several other HIF-PH inhibitor 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 companies such as FibroGen Inc., or FibroGen, together with its collaboration partners, Astellas Pharma Inc. and AstraZeneca PLC, Japan Tobacco International, or JT, and Bayer HealthCare AG, or Bayer. For example, FibroGen filed an NDA for its product candidate, roxadustat, with the FDA, but the FDA issued a complete response letter indicating the FDA will not approve the NDA in its present form and requested that an additional clinical trial for roxadustat be conducted prior to resubmission of the NDA or additional response to the FDA's complete response letter. In Europe however, roxadustat is approved for the treatment of anemia in patients with CKD. If we obtain approval for vadadustat in the U.S., and roxadustat is also approved by the FDA, then roxadustat will compete with vadadustat.

Furthermore, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce injectable erythropoiesis stimulating agent, or 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.

In Japan, Vafseo, which is approved for both the DD and NDD indications, competes with roxadustat, daprodustat and enarodustat. Roxadustat is approved for the treatment of anemia due to CKD in patients on dialysis, or DD-CKD, and patients not on dialysis, or NDD-CKD. In addition, daprodustat, GSK's product, and enarodustat, JT's product, are approved in Japan for the treatment of anemia due to CKD. In addition. Bayer HealthCare AG has submitted an NDA for its product candidate for the treatment of renal anemia in Japan. In China, roxadustat is commercialized for the treatment of anemia of DD-CKD and for the treatment of anemia due to CKD in NDD-CKD patients.

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 vadadustat. 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 and several biosimilar versions of injectable ESAs are available for sale in the EU.

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, Roche and GSK, 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™ and Vafseo™ in Japan, Vafseo™ in Europe and our current and potential 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 Pharmaceutical Co., Ltd., or Torii, commercialize Riona, the trade name for ferric citrate hydrate in Japan, as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and for the treatment of adult patients with IDA in Japan. In Japan and certain other countries in Asia, we granted MTPC exclusive rights to commercialize vadadustat, which has been approved and is being marketed by MTPC in Japan under the trade name Vafseo™. We also granted Averoa SAS, or Averoa, an exclusive license to develop and commercialize ferric citrate in the EEA, Turkey, Switzerland and the United Kingdom.

Pursuant to the terms of the Termination Agreement with Otsuka, Otsuka has transferred to us the marketing authorization application, or MAA, for vadadustat with the EMA, and in the United Kingdom, Switzerland and Australia, and in April 2023, the European Commission, or EC, approved the marketing authorization of Vafseo™.. In addition, we have conducted and in the future plan to conduct clinical trials outside of the United States for Auryxia, vadadustat and any other product or product candidate that may be in-licensed or acquired. As a result of these and other activities, we are or may become subject to additional risks in developing and commercializing Auryxia and vadadustat outside the United States, including, among others:

- political, regulatory, compliance and economic developments, weakness or instability that could restrict our ability to manufacture, market and sell our products;
- changes in international medical reimbursement policies and programs;
- changes in healthcare policies of foreign jurisdictions;
- trade protection measures, including import or export licensing requirements and tariffs and our compliance therewith;
- our ability to develop or manage relationships with qualified local distributors and trading companies;
- diminished protection of intellectual property in some countries outside of the United States;
- differing labor regulations and business practices;
- compliance with laws, including the U.S. Foreign Corrupt Practices Act, or FCPA, the UK Bribery Act or similar local regulation, the EU General Data Protection Regulation, or GDPR, and similar data protection laws, and tax, employment, immigration and labor laws;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad, including as a result of the COVID-19 pandemic; and
- business interruptions resulting from geopolitical actions, including war and terrorism, global pandemics, or natural disasters including earthquakes, typhoons, floods and fires.

In addition, we receive revenues from royalty payments converted to U.S. dollars based on net sales of Riona and Vafseo™ in Japanese yen. The exchange rates between the Japanese yen on the one hand, and the U.S. dollar, on the other hand, have changed substantially in recent years and may fluctuate substantially in the future. Our results of operations could be adversely affected over time by certain movements in exchange rates, particularly if the Japanese yen depreciates against the U.S. dollar.

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 Product Development

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and, if approved, commercialization of vadadustat and any other product candidates.

The risk of failure in drug development is high. 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. Preclinical studies and 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 process.

We may be unable to successfully complete clinical trials of Auryxia, vadadustat and other product candidates or to successfully obtain approval of vadadustat or other product candidates, 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. 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, interim results of a clinical trial do not necessarily predict final results, and results of Phase 3 clinical trials for one indication may not be predictive of results of Phase 3 clinical trials for another indication. For example, we announced positive top-line results from $INNO_2VATE$ and vadadustat achieved the primary and key secondary efficacy endpoint in each of the two PRO_2TECT studies, but the PRO_2TECT program did not meet the primary major adverse cardiovascular event, or MACE, safety endpoint. 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. 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. In addition, in March 2022, we received the CRL for vadadustat indicating that the FDA had determined that it could not approve the NDA in its present form, thus delaying any potential approval of vadadustat. In October 2022, we submitted the FDRR to the FDA and in February 2023, we received a second interim response from the FDA to our FDRR. However, it is impossible to predict when or if vadadustat or any of our other product candidates will prove effective or safe in humans or will receive marketing approval or on what terms. In April 2023, the EC approved Vafseo™ (vadadustat), an oral HIF-PH inhibitor, for the treatment of symptomatic anemia associated with CKD in adults on chronic maintenance dialysis. However, we do not have commercial operations in Europe. We plan to pursue a new partner to commercialize vadadustat in Europe and other territories previously licensed to Otsuka. If we are unsuccessful in entering into a new agreement for the commercialization of vadadustat in Europe in a timely manner, or at all, it may result in a delay in the launch of vadadustat in Europe, and could have an adverse effect on our results of operations.

We may experience numerous unforeseen events during, or as a result of, preclinical development or clinical trials that could delay, prevent or make more challenging our ability to receive or maintain marketing approval or commercialize our product candidates. We may be required to complete additional clinical trials for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, in order to obtain or maintain required regulatory approvals. Our preclinical studies and 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 needed to obtain or maintain regulatory approval for a variety of other reasons, such as:

- the costs may be greater than we anticipate;
- the number of patients required for clinical trials may be larger than we anticipate;
- enrollment in our clinical trials 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 CROs, 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, independent 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 or results that may be interpreted in a manner different than we interpret them, 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;
- we may fail 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 PMDA, or other regulatory authorities, or for other reasons, such as failure to recruit or enroll suitable patients or patients' failure to return for post-treatment follow up;
- 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;
- there may be an 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;
- there may be a delay or failure in reaching agreement with the FDA, the EMA, the PMDA or other regulatory authorities on a clinical trial design upon which we are able to execute;
- there may be a 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;
- there may be 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, the 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, the 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;

- third parties with which we work may fail to comply with good practice quality guidelines and regulations, or GXP, including good laboratory practice, good clinical practice, or GCP, and current good manufacturing practice, or cGMP; or
- there may be changes in governmental regulations or administrative actions.

If any of the foregoing occurs, the following may occur:

- regulators may require that we conduct additional clinical trials, repeat clinical trials or conduct other studies beyond those that we currently contemplate;
- we may be delayed in obtaining marketing approval for vadadustat or other product candidates;
- we may not obtain marketing approval for vadadustat or other 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 any approved product or inhibit our ability to successfully commercialize any approved product;
- a REMS or FDA-imposed risk management plan that use risk minimization strategies to ensure that the benefits of certain prescription drugs outweigh their risks, may be required;
- 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 may also increase if we experience development delays or delays in 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 vadadustat, if approved, or any other product candidate, including those that may be in-licensed or acquired, 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.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.

Identifying and qualifying patients to participate in clinical trials is critical to our success. The timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our clinical trials. Patients may be unwilling to participate in our clinical trials because of concerns about investigational research studies, the time and commitment needed to participate in a study, adverse events observed with the product candidate under study, the current standard of care, competitor products and/or other investigational agents, in each case for the same indications and/or similar patient populations. In addition, in the case of clinical trials of any product candidate, patients currently receiving treatment with the current standard of care or a competitor product may be reluctant to participate in a clinical trial with an investigational drug. Additionally, it is often more difficult to enroll special or particular subpopulations of patients, such as pediatric or elderly patients, due to a number of factors including parental or other caregiver considerations, concerns and burdens. For example, we enrolled sites in a post-approval pediatric study for the Hypophosphatemia Indication of Auryxia in the second quarter of 2022, which began patient recruitment in the third quarter of 2022, but study sites have not yet enrolled any eligible pediatric patients despite efforts to do so. Furthermore, the COVID-19 pandemic resulted in temporary closures of, and may continue to impact, clinical trial sites on which we rely for the conduct of clinical trials and COVID-19 pandemic precautions and staffing shortages have caused moderate delays in enrolling new clinical trials and may cause delays in enrolling other new clinical trials.

Finally, competition for clinical trial sites may limit our access to patients appropriate for our clinical trials. As a result, the timeline for recruiting patients and conducting studies may be delayed. These delays could result in increased costs, delays in advancing our development of any product or product candidate, or termination of the clinical trial 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 trials 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, including study complexity;
- perceived risks and benefits of the product or product candidate under study, including as a result of adverse effects observed in similar or competing therapies;

- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product or product candidate being studied in relation to available therapies or other product candidates in development;
- efforts to facilitate timely enrollment in clinical trials;
- participation length and demands on patients and caregivers;
- site staffing shortages and turnover;
- clinical trial sites and investigators failing to perform effectively; and
- patient referral practices of physicians.

We may not be able to initiate or complete clinical trials in a timely manner, or at all, if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which may delay approval, or result in failure to maintain or obtain approval, of our products or product candidates, which would have a material adverse effect on our business.

Further, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. For example, in December 2022, with the passage of Food and Drug Omnibus Reform Act, Congress required sponsors to develop and submit a diversity action plan for each phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products.

Conducting clinical trials outside of the United States, as we have done historically and as we may decide to do in the future, presents additional risks and complexities and, if we decide to conduct a clinical trial outside of the United States in the future, we may not complete such trials successfully, in a timely manner, or at all, which could affect our ability to obtain regulatory approvals.

Our ability to successfully initiate, enroll and complete a clinical trial 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;
- difficulty in complying with different local standards for the conduct of clinical trials;
- 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, the 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. Further, when a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee, and seeking and receiving informed consent from subjects. Thus, to the extent that we rely on data from foreign clinical trials that are not the subject of an IND but are used to support of an NDA, there is a risk that FDA may not review such data in connection with its review of the NDA.

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

Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, may cause undesirable side effects or have other properties that may delay or prevent marketing approval or limit their commercial potential.

Undesirable effects caused by, or other undesirable properties of, Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, or competing commercial products or product candidates 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. In addition, results of our clinical trials could reveal a high frequency of undesirable effects or unexpected characteristics. For example, in March 2022, we received the CRL from the FDA for our NDA for vadadustat in which the FDA concluded that the data in the NDA do not support a favorable benefit-risk assessment of vadadustat for dialysis and non-dialysis patients. The FDA expressed safety concerns noting failure to meet non-inferiority in MACE in the non-dialysis patient population, the increased risk of thromboembolic events, driven by vascular access thrombosis in dialysis patients, and the risk of drug-induced liver injury. In October 2022, we submitted the FDRR to the FDA. The FDRR focuses on the favorable balance between the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult patients on dialysis in light of safety concerns expressed by the FDA in the CRL for dialysis patients related to the rate of adjudicated thromboembolic events driven by vascular access thrombosis for vadadustat compared to the active comparator and the risk of drug-induced liver injury. In February 2023, we received a second interim response from the FDA to our FDRR, and there can be no assurances that we will be successful in our appeal. If we are unable to overcome these concerns, vadadustat may not be approved by the FDA on favorable terms, or at all, and our financial condition could be materially harmed.

If we or others identify undesirable effects caused by, or other undesirable properties of, Auryxia, vadadustat, or any other product or product candidate, including those that may be in-licensed or acquired, or if known undesirable effects are more frequent or severe than in the past, 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:

- our product candidates may not be approved by regulatory authorities;
- our clinical trials may be put on hold;
- patient recruitment could be slowed, and enrolled patients may not want to complete the clinical trial;
- regulatory authorities may require warnings on the label, such as the warning on Auryxia's label regarding iron overload;
- REMS or FDA-imposed risk management plans that use restrictive risk minimization strategies may be required;
- we may decide to, or be required to, send drug warnings or safety alerts to physicians, pharmacists and hospitals (or the FDA or other regulatory authorities 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 non-clinical or clinical trials, restrictive 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
- we could be investigated by the government or sued and held liable for harm caused to patients, including in class action lawsuits; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining, whether on a restricted basis or at all, marketing approval and, ultimately, market acceptance or penetration of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired. In addition, any of these events could substantially increase our costs, and could significantly impact our ability to successfully commercialize Auryxia, vadadustat or any other product and product candidate, including those that may be in-licensed or acquired, and generate product revenue.

The patient populations treated with Auryxia and potential patient populations for vadadustat, if approved, have CKD, a serious disease that increases the risk of cardiovascular disease including heart attacks and stroke and, in its most severe form, results in, kidney failure and the need for dialysis or kidney transplant. Many patients with CKD are elderly with comorbidities making them susceptible to significant health risks. Therefore, the likelihood of these patients having adverse events, including serious adverse events is high.

With respect to the global INNO$_2$VATE Phase 3 program, the incidence of treatment emergent adverse events during the *Correction and Conversion* study in vadadustat treated patients was 83.8% and 85.5% in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa treated patients were hypertension (16.2%/ 12.9%) and diarrhea (10.1%/ 9.7%). Serious treatment emergent adverse events were lower in vadadustat treated patients at 49.7% compared to 56.5% for darbepoetin alfa treated patients. The incidence of treatment emergent adverse events during the prevalent dialysis patient study (*Conversion*) in the vadadustat treated patients was 88.3%, and 89.3% in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa treated patients were diarrhea (13.0%/ 10.1%), pneumonia (11.0%/ 9.7%), hypertension (10.6%/ 13.8%), and hyperkalemia (9.0%/ 10.8%). Serious treatment emergent adverse events were slightly lower for vadadustat treated patients at 55.0% and 58.3% for darbepoetin alfa-treated patients. Patients with DD-CKD experienced an increased risk of

thromboembolic events compared to darbepoetin alfa with a time to first event HR of 1.20 (95% CI 0.96 - 1.50) driven by thrombosis of vascular access.

With respect to the global PRO_2TECT Phase 3 program, the incidence of treatment emergent adverse events during the erythropoiesis stimulating agent, or ESA, untreated patients study (*Correction*) in the vadadustat-treated patients was 90.9%, and 91.6% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (34.7%/ 35.2%), hypertension (17.7%/ 22.1.%), hyperkalemia (12.3.%/ 15.6%), urinary tract infection (12.9%/ 12.0%), diarrhea (13.9%/ 10.0%), peripheral oedema (12.5%/ 10.5%), fall (9.6%/ 10%) and nausea (10%/ 8.2%). Serious treatment emergent adverse events were 65.3% for vadadustat-treated patients and 64.5% for darbepoetin alfa-treated patients. The incidence of treatment emergent adverse events during the ESA-treated patients study (*Conversion*) in vadadustat treated patients was 89.1% and 87.7% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (27.5%/ 28.4%), hypertension (14.4%/ 14.8%), urinary tract infection (12.2%/ 14.5%), diarrhea (13.8.%/ 8.8.%), peripheral oedema (9.9%/ 10.1%) and pneumonia (10.0%/ 9.7%). Serious treatment emergent adverse events were 58.5% for vadadustat-treated patients and 56.6% for darbepoetin alfa-treated patients.

For example, during the conduct of our Phase 3 program our team and hepatic experts analyzed hepatic cases (unblinded to treatment) and, following the completion of our global Phase 3 clinical program for vadadustat, there was a review of hepatic safety across the vadadustat clinical program, which included eight completed Phase 2 and 3 studies in NDD-CKD patients, 10 completed Phase 1, 2, and 3 studies, and two then-ongoing Phase 3b studies in DD-CKD patients, and 18 completed studies in healthy subjects (17 Phase 1 and one Phase 3). This review consisted of a blinded re-assessment of hepatic events conducted by a separate panel of hepatic experts. While hepatocellular injury attributed to vadadustat was reported in less than 1% of patients, there was one case of severe hepatocellular injury with jaundice, and we cannot guarantee that similar events will not happen in the future. Additionally, the FDA expressed safety concerns related to the risk of drug-induced liver injury in the CRL that it issued in March 2022.

Serious adverse events considered related to vadadustat, including those noted in the CRL, and any other product candidates could have material adverse consequences on the development and potential approval of vadadustat or our other 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, the FDA may not agree with our assessment of adverse events and additional unexpected adverse events may be observed in future clinical trials or in the market.

Any of the above safety data or other occurrences could delay or prevent us from achieving or maintaining marketing approval, harm or prevent sales of Auryxia or, if approved, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, increase our expenses and impair or prevent our ability to successfully commercialize Auryxia, vadadustat or any other products or product candidates.

In addition, any post-marketing clinical trials conducted, if successful, may expand the patient populations treated with Auryxia, vadadustat or any other product 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 undesirable effects, increased frequency or severity of known undesirable effects, or result in the identification of unexpected safety signals. In addition, as vadadustat, if approved, and any other products are commercialized, they will be used in significantly larger patient populations, in less rigorously controlled environments and, in some cases, by less experienced and less expert treating practitioners, than in clinical trials, which could result in increased or more serious adverse effects being reported. As a result, regulatory authorities, healthcare practitioners, third party payors or patients may perceive or conclude that the use of Auryxia, vadadustat, if approved, or any other products are associated with serious adverse effects, undermining our commercialization efforts.

Risks Related to Regulatory Approval

We may not be able to obtain marketing approval for, or successfully commercialize, vadadustat or any other product candidate, or we may experience significant delays in doing so, any of which would materially harm our business.

Clinical trials, manufacturing and marketing of any product or product candidate are subject to extensive and rigorous review and regulation by numerous governmental authorities in the United States and other jurisdictions. 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

and commercialization efforts, we may be unable to successfully obtain regulatory approval for or commercialize vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.

We are not permitted to market vadadustat in the United States until we receive approval from the FDA 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 may be required by the FDA or other regulatory authorities to conduct additional preclinical studies or clinical trials.

In March 2022, we received the CRL from the FDA regarding our NDA for vadadustat for the treatment of anemia due to CKD. The FDA concluded that the data in the NDA do not support a favorable benefit-risk assessment of vadadustat for dialysis and non-dialysis patients. In October 2022, we submitted a Formal Dispute Resolution Request, or FDRR, to the FDA. The FDRR focuses on the favorable balance between the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult patients on dialysis in light of safety concerns expressed by the FDA in the CRL for dialysis patients related to the rate of adjudicated thromboembolic events driven by vascular access thrombosis for vadadustat compared to the active comparator and the risk of drug-induced liver injury. In February 2023, we received a second interim response from the FDA to our FDRR, and there can be no assurances that we will be successful in our appeal and obtain approval for vadadustat in a timely manner, on favorable terms, or at all. As a result, the regulatory approval process for vadadustat in the U.S. is highly uncertain. We may not obtain approval at all, and if we are able to obtain approval, it may only be for patients with DD-CKD and, in any event, the expense and time to do so could adversely impact our ability to successfully commercialize vadadustat, and our financial condition could be materially harmed.

Further, vadadustat and any other product candidate may not receive marketing approval in the United States even if it is approved in other countries. For example, although vadadustat is approved in Japan for the treatment of anemia due to CKD in DD-CKD and NDD-CKD adult patients and in Europe for the treatment of aneumia due to CKD in DD-CKD patients, such approval does not guarantee approval in the United States by the FDA for these indications or at all. In addition, while each regulatory authority makes their own assessment as to the safety and efficacy of a drug, FDA's concern about the safety or efficacy of vadadustat or any other product candidate could impact the regulatory authority's decision in another country.

Obtaining marketing approval in the United States and other jurisdictions for any product candidate depends upon numerous factors, many of which are subject to the substantial discretion of the regulatory authorities, including that regulatory agencies may not complete their review processes in a timely manner and, following completion of the review process, may not grant marketing approval or such marketing approval may be limited. Furthermore, approval of a drug does not ensure successful commercialization. For example, on September 23, 2015, the European Commission, or EC, approved Fexeric for the control of hyperphosphatemia in adult patients with CKD. Pursuant to the sunset clause under EU law, the EC's approval of Fexeric in the EU was contingent on, among other things, our commencing marketing of Fexeric within three years; although we successfully negotiated an extension to December 23, 2019, we did not commence marketing Fexeric by such date and therefore the Fexeric approval in the EU has ceased to be valid.

We could face heightened risks with respect to seeking marketing approval in the United Kingdom, or UK, as a result of the recent withdrawal of the UK from the EU, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the UK and the EU, the UK withdrew from the EU, effective December 31, 2020. On December 24, 2020, the UK and the EU entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement would prevent us from commercializing vadadustat or any other product candidate, including those that may be in-licensed or acquired, in the UK and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the UK for vadadustat or any other product candidate, which could significantly and materially harm our business. As of January 1, 2021, the Medicines and Healthcare Products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended) as the basis for regulating medicines.

In addition, the safety concerns associated with the current standard of care for the indications for which we are seeking marketing approval for vadadustat may affect the FDA's or other regulatory authorities' review of the safety results of vadadustat. Additionally, these regulatory authorities may not agree with our assessment of adverse events. 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 will never obtain marketing approval in the United States or certain other jurisdictions or for some or all of the indications for which we seek approval. The FDA or other regulatory authorities may delay, limit or deny approval of vadadustat for many reasons including, among others:

- we may not be able to demonstrate that vadadustat is safe and effective in treating adult patients with anemia due to CKD to the satisfaction of the relevant regulatory authority;
- 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 results of our clinical trials may not meet the level of statistical or clinical significance required by the relevant regulatory authority for review and/or marketing approval;
- the relevant regulatory authority may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the relevant regulatory authority may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the relevant regulatory authority may not approve the formulation, labeling or specifications we request for vadadustat;
- the relevant regulatory authority 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 relevant regulatory authority may require that we conduct additional clinical trials or repeat one or more clinical trials;
- the FDA or other relevant regulatory authority may require development of a REMS as a condition of approval or post-approval;
- the relevant regulatory authority may grant approval contingent on the performance of costly post-marketing clinical trials;
- the relevant regulatory authority's onsite inspections may be delayed due to the COVID-19 pandemic or otherwise;
- we, or our CROs or other vendors, may fail to comply with GXP or fail to pass any regulatory inspections or audits;
- we or our third party manufacturers may fail to perform in accordance with the FDA's or other relevant regulatory authority's cGMP requirements and guidance;
- 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 relevant regulatory authority 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;
- as part of any future regulatory process, the FDA may ask an Advisory Committee to review portions of the NDA, the FDA may have difficulty scheduling an Advisory Committee meeting in a timely manner or, if convened, an FDA Advisory Committee could recommend non-approval, conditions of approval or restrictions on approval, and the FDA may ultimately agree with the recommendations;
- the relevant regulatory authority's review process and decision-making regarding vadadustat and any other product candidate may be impacted by the results of our and our 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 candidate are being developed;
- the relevant regulatory authority may not approve the manufacturing processes or facilities of third party manufacturers with whom we contract; or
- the policies or regulations of the relevant regulatory authority may significantly change in a manner that renders our clinical data insufficient for approval or requires us to amend or submit new clinical protocols.

If we experience further delays in obtaining approval, or if we fail to obtain approval of vadadustat for some or all of the indications for which we have sought approval, the commercial prospects for vadadustat may be harmed and our ability to generate revenues will be materially impaired, which could have a material adverse effect on our business. For example, the FDRR we submitted to the FDA in October 2022 focuses on the favorable balance between the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult patients on dialysis.

Finally, our ability to develop and market new drug products may be threatened by ongoing litigation challenging the FDA's approval of mifepristone. Specifically, on April 7, 2023, the U.S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a REMS. In reaching that decision, the district court made a number of findings that numerous representatives of the pharmaceutical and biotechnology industry believe will chill the development, approval and distribution of new drug products in the United States. Among other determinations, the district court substituted its scientific judgement for that of the FDA and it held that FDA must provide a special justification for any differences between an approved drug's labeling and the conditions that existed in the drug's clinical trials. Further, the district court read the jurisdictional requirements governing litigation in federal court so as to potentially allow virtually any party to bring a lawsuit against the FDA in connection with its decision to approve an NDA or establish requirements under a REMS. On April 13, 2023, the district court decision was stayed, in part, by the U.S. Court of Appeals for the Fifth Circuit. Thereafter, on April 21,

2023, the US Supreme Court entered a stay pending disposition of the appeal of the district court decision in the Court of Appeals for the Fifth Circuit or the Supreme Court. Depending on the outcome of this litigation and the regulatory uncertainty it has engendered, our ability to develop new drug product candidates and to maintain approval of existing drug products and measures adopted under a REMS is at risk and could be delayed, undermined or subject to protracted litigation.

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, including withdrawal of marketing approval, if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, or product candidates, 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 or commitments 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 of 2003, or PREA. With regard to the Hyperphosphatemia Indication for Auryxia, we initially committed to completing the original post-approval pediatric study and submitting a final report to the FDA by December 31, 2019. However, we did not complete the study according to the original schedule and therefore did not submit the required final report by December 31, 2019. Consequently, we received a notification of noncompliance with PREA. However, we have since been released from the original post marketing requirement, or PMR, and a new PMR was issued. Therefore, this PMR trial is no longer considered delayed. Recruitment of the other patients is pending receipt of further data regarding the manufacturing of the smaller size tablets and the FDA's concurrence before proceeding with the use of such formulation. With regard to our IDA Indication, we initially committed to completing the post-approval pediatric study and submitting a final report to the FDA by January 2023. We did not meet a milestone relating to this post-approval pediatric study of Auryxia in a timely manner and received a notification from the FDA. Subsequently, the FDA agreed to extend the pediatric clinical trial timelines for the IDA Indication. We subsequently communicated to the FDA that we would be delaying the start of the clinical trial in the IDA Indication while we work to produce smaller size tablets. In response, the FDA issued a partial clinical hold until we manufacture the smaller tablets and provide the FDA with relevant information regarding the smaller sized tablets for review. The FDA lifted the partial clinical hold in June 2022, however, we have not commenced start up of this study pending resolution of the manufacturing of the smaller size tablets. If we are unable to complete these studies successfully, or have further delays in completing these studies, we will need to inform the FDA, have further discussions and, if the FDA finds that we failed to comply with pediatric study requirements, in violation of applicable law, it could institute enforcement proceedings to seize or enjoin the sale of Auryxia or seek civil penalties, 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, vadadustat, if approved, and any other product for which we receive regulatory approval will be subject to extensive and ongoing regulatory requirements and guidance. These requirements and guidance include manufacturing processes and procedures (including record keeping), the implementation and operation of quality systems to control and assure the quality of the product, 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. If we, our CMOs or other third parties we engage fail to adhere to such regulatory requirements and guidance, we could suffer significant consequences, including product seizures or recalls, loss of product approval, fines and sanctions, reputational damage, loss of customer confidence, shipment delays, inventory shortages, inventory write-offs and other product-related charges and increased manufacturing costs, and our development or commercialization efforts may be materially harmed.

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 any approved product beyond its 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 FDCA, 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, insurance fraud laws, third party payor actions, stockholder 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.

For example, we previously had three limited, voluntary recalls of Auryxia. These and any other recalls or any supply, quality or manufacturing issues in the future could result in significant negative consequences, including reputational harm, loss of customer confidence, and a negative impact on our financials, any of which could have a material adverse effect on our business and results of operations, and may impact our ability to supply Auryxia, Vafseo™, in Japan or vadadustat, if approved, for commercial and clinical use.

Non-compliance with the FDA, the EMA, the 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.

Risks Related to Governmental Regulation and Compliance

We are subject to a complex regulatory scheme that requires significant resources to ensure compliance and our failure to comply with applicable laws could subject us to government scrutiny or enforcement, potentially resulting in costly investigations, fines, penalties or sanctions, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

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

- laws and regulations governing the conduct of preclinical studies and clinical trials in the United States and other countries in which we are conducting such studies;
- 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, the UK 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, state privacy and data protection laws, such as the California Consumer Privacy Act, or CCPA, and the California Privacy Rights Act of 2020, or CPRA, as well as state consumer protection laws, GDPR, any additional applicable EU member state data protection laws in force from time to time, the retained EU law version of the General Data Protection Regulation as saved into United Kingdom law by virtue of section 3 of the United Kingdom's European Union (Withdrawal) Act 2018, or the EU GDPR;
- federal and state laws requiring the submission of accurate product prices and notifications of price increases;
- federal and state securities laws;
- environmental, health and safety laws and regulations; 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.

In addition, our relationships with healthcare providers, physicians and third party payors expose us to broadly applicable fraud and abuse laws that may constrain the business or financial arrangements and relationships through which we market, sell and distribute Auryxia and vadadustat, if approved, and any other products for which we may obtain marketing approval. As such, these arrangements are subject to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations at federal, state and international levels. These restrictions include, but are not limited to, the following:

- the FDCA 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, which 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, which 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, and violations of the FDCA, the federal government pricing laws, and the federal Anti-Kickback Statute trigger liability under the federal False Claims Act;
- HIPAA, which 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 (renamed the Open Payments Act) requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and gift ban and transparency statutes, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by state Medicaid or other programs, or 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, which vary from state to state.

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 Statute. 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.

Efforts to ensure that our business complies with applicable healthcare laws and regulations involves substantial costs and requires us to expend significant resources. One of the potential areas for governmental scrutiny involves federal and state requirements for pharmaceutical manufacturers to submit accurate price reports to the government. Because our processes for calculating applicable government prices and the judgments involved in making these calculations involve subjective decisions and complex methodologies, these calculations are subject to risk of errors and differing interpretations. In addition, they are subject to review and challenge by the applicable governmental agencies, or potential qui tam complaints, and it is possible that such reviews could result in changes, recalculations, or defense costs that may have adverse legal or financial consequences. 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, any of which could materially adversely affect our business and would result in increased costs and diversion of management attention and could negatively impact the development, regulatory approval and commercialization of Auryxia or vadadustat, any of which could have a material adverse effect on our business. Further, 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.

We will incur significant liability if it is determined that we are promoting any "off-label" use of Auryxia or any other product we may develop, in-license or acquire 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 FDCA 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, the Department of Justice 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 September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. 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 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. It may also be subject to exclusion and debarment from federal healthcare reimbursement programs.

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 guidance 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, such program and processes may not be sufficient to deter or detect all violations.

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, employees, and other representatives could be subject to significant fines and criminal sanctions, imprisonment, and potential exclusion from Medicare and Medicaid, and could harm our reputation or result in significant legal expenses and distraction of management.

Disruptions in the FDA, regulatory authorities outside the U.S. and other government agencies caused by global health concerns or funding shortages could prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA and regulatory authorities outside the U.S. to review and approve new products can be affected by a variety of factors, including global health concerns, government budget and funding levels, staffing shortages, statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's or other regulatory authorities' ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result of certain of these factors. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may increase the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our

business. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our, or our collaboration partners', regulatory submissions, which could have a material adverse effect on our business.

Disruptions may result also from continuation of the COVID-19 pandemic or any similar event that may occur in the future. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. The FDA has now indicated that it can and will conduct timely reviews of applications for medical in line with its user fee performance goals, including conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, in the event of a resurgence of the COVID-19 pandemic or a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the United States facing similar circumstances may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may also experience delays in their regulatory activities.

If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Compliance with 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 EEA, in May 2018. Following the withdrawal of the U.K. from the EU, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the U.K. and includes parallel obligations to those set forth by GDPR. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data when required, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, when required, 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 as a sponsor in clinical trials 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 patients and investigators. 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 and permits EU member states to adopt further penalties for violations that are not subject to the administrative fines outlined in the GDPR.

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 we 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. There is ongoing uncertainty about the transfer mechanisms that companies rely upon to enable the legal transfer of personal data from the EU to other countries. For example, in July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. As court decisions and regulatory guidance evolves, challenges remain with respect to GDPR compliance. Companies must continue to monitor the regulatory landscape and implement necessary changes, all of which may be costly and may put the company out of compliance while any changes are being implemented.

Given the breadth and depth of changes in data protection obligations, 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.

Similar privacy and data security requirements are either in place or underway in the United States. There are a broad variety of data protection laws that may be applicable to our activities, and a range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the CCPA, which went into effect on January 1, 2020, and the CPRA, which amends CCPA by expanding the scope and applicability, while also introducing new privacy protections, is creating similar risks and obligations as those created by GDPR. The CPRA also creates a new agency that is specifically responsible for enforcing the new law. Because of this, we may need to engage in additional activities (e.g., data mapping) to identify the personal information we are collecting and the purposes for which such information is collected. In addition, we will need to ensure that our policies recognize the rights granted to consumers (as that phrase is broadly defined in the CCPA and can include business contact information). Other states have also passed privacy laws that are similar to the CCPA/CPRA, including Virginia, Colorado, Connecticut, and Utah. The laws in the various states vary in terms of their exact requirements, but they all provide regulators in these states with enforcement authority. Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with current and any future federal and state laws regarding privacy and security of personal information could expose us to fines and penalties. We also face a threat of potential consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Legislative and regulatory healthcare reform 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 vadadustat, or any other product candidate, restrict or regulate post-approval activities and affect our ability to profitably sell Auryxia and vadadustat, if approved. 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 or vadadustat, if approved, or any reimbursement that physicians receive for administering any approved product.

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. In addition, other legislative changes and regulatory 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 2031. However, pursuant to the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, and subsequent legislation, these Medicare sequester reductions were suspended and reduced through the end of June 2022, but the full 2% cut resumed as of July 1, 2022.

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. In addition, other legislative and regulatory changes have been proposed, but not yet adopted. For example, in July 2019, HHS proposed regulatory changes in kidney health policy and reimbursement. Any new legislative or regulatory changes may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for Auryxia or vadadustat, if approved, or the frequency with which Auryxia and vadadustat, if approved, is prescribed or used.

The costs and prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. 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.

For example, the former administration issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

At the same time, the administration may seek to limit Medicare Part D and public option drug prices through a tax penalty on manufacturers for increases in the cost of drugs and biologics above the general inflation rate. The American Rescue Plan Act of 2021, comprehensive COVID-19 pandemic relief legislation recently enacted under the current administration, includes a number of healthcare-related provisions, such as support to rural health care providers, increased tax subsidies for health insurance purchased through insurance exchange marketplaces, financial incentives to states to expand Medicaid programs and elimination of the Medicaid drug rebate cap effective in 2024.

Further, on July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs HHS to create a plan within 45 days to combat “excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging.” On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

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. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare 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 healthcare 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.

In addition, in some countries, including member states of the 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 and/or 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 and/or product candidates 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.

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

We depend on collaborations with third parties for the development and commercialization of Auryxia, Riona, Vafseo and vadadustat and if these 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, Riona, Vafseo and vadadustat, and our business could be materially harmed.

We sublicensed the rights to commercialize Riona to JT and Torii in Japan. We also entered into a collaboration agreement with MTPC to develop and commercialize vadadustat in Japan and certain other Asian countries. In addition, we entered into the Vifor Second Amended Agreement pursuant to which we granted CSL Vifor an exclusive license to sell vadadustat to the

Supply Group in the United States. We also granted to Averoa an exclusive license to develop and commercialize ferric citrate in the EEA, Turkey, Switzerland and the United Kingdom. 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 and our partners' commercialization efforts with respect to Auryxia, Riona, Vafseo and our and our partners' development and, if approved, commercialization efforts with respect to vadadustat and any other product candidates. We may not be able to maintain our collaborations for development and commercialization. For example, on May 13, 2022, Otsuka elected to terminate our collaboration agreements with them, and we subsequently negotiated the Termination Agreement with Otsuka. This termination by Otsuka may delay the launch of vadadustat in Europe or the approval or launch of vadadustat in other territories or adversely affect how we are perceived in scientific and financial communities. In addition, our current and any future 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 collaboration agreements 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 collaboration agreements, 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 collaboration agreements, 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 to our products may not commit sufficient resources to their marketing and distribution;
- if permitted by the terms of the collaboration agreements, we and our collaborator may have a difference of opinion regarding the development or commercialization strategy for a particular product or product candidate, 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, supply or commercialization of Auryxia, Riona, Vafseo or vadadustat and any other product candidate, 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, if approved, 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 and legal requirements.

If any of these events occurs, the market potential of Auryxia, Riona, Vafseo or vadadustat, if and where approved, and any other products or product candidates, could be reduced, and our business could be materially harmed. Collaborations may also divert resources, including the attention of management and other employees, from other parts of our business, which could have an adverse effect on other parts of our business, and we cannot be certain that 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, or at all, 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 any of our product candidates, including vadadustat, if approved, especially following the termination of our collaboration agreements with Otsuka. We may decide to enter into additional collaborations for the development and commercialization of vadadustat or Auryxia, both within and outside of the United States. For example, we plan to pursue a new partner to develop and commercialize vadadustat in Europe and other territories previously licensed to Otsuka. If we are unsuccessful in entering into a new agreement for the development and commercialization of vadadustat in Europe and other territories in a timely manner, or at all, it may result in a delay in the launch of vadadustat in Europe or the approval or launch of vadadustat in other territories, a need for additional capital and expansion of our internal capabilities to pursue further development or commercialization of the applicable products and product candidates, particularly the development and commercialization of vadadustat in Europe and other territories, and could have an adverse effect on our results of operations. 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, divert management’s attention, or disrupt our 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;
- an inability to negotiate collaborations on acceptable terms, on a timely basis or at all;
- any international rules, regulations, guidance, laws, risks or uncertainties with respect to potential partners outside of the United States;
- a potential collaborator's evaluation of Auryxia, vadadustat or any other product or product candidate may differ substantially from ours;
- a potential collaborator's evaluation of our financial stability and resources;
- a potential collaborator's resources and expertise; and
- restrictions due to an existing collaboration agreement.

If we are unable to enter into additional collaborations in a timely manner, or at all, we may have to delay or curtail the commercialization of Auryxia or vadadustat, if and where approved, reduce or delay its development program or other of our other development programs, or increase our expenditures and undertake additional 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 develop or commercialize Auryxia or vadadustat, if approved.

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.

Royalties from commercial sales of vadadustat under our MTPC Agreement will likely fluctuate and will impact our rights to receive future payments under our Royalty Agreement with HCR.

Pursuant to the Royalty Agreement with HCR, we sold to HCR our right to receive the Royalty Interest Payments payable to us under the MTPC Agreement, subject to the Annual Cap and the Aggregate Cap. After HCR receives Royalty Interest Payments equal to the Annual Cap in a given calendar year, we will receive 85% of the Royalty Interest Payments for the remainder of that year. After HCR receives Royalty Interest Payments equal to the Aggregate Cap, or we pay the Aggregate Cap to HCR (net of the Royalty Interest Payments already received by HCR), the Royalty Interest Payments will revert back to us, and HCR would have no further right to any Royalty Interest Payments. We received $44.8 million from HCR (net of certain transaction expenses) under the Royalty Agreement, and we are eligible to receive up to an additional $15.0 million under the Royalty Agreement if specified sales milestones are achieved for vadadustat in the territory covered by the MTPC Agreement, subject to the satisfaction of certain customary conditions.

The royalty revenues under the MTPC Agreement may fluctuate considerably because they depend upon, among other things, the rate of growth of sales of vadadustat in the territory covered by the MTPC Agreement. Negative fluctuations in these royalty revenues could delay, diminish or eliminate our right to receive up to the additional $15.0 million under the Royalty Agreement upon achievement of the specified sales milestones, our ability to receive 85% of the Royalty Interest Payments after the Annual Cap is achieved in a given calendar year, or our ability to receive 100% of the Royalty Interest Payments after the Aggregate Cap is achieved.

We rely upon third parties to conduct all aspects of our product manufacturing, and in many instances only have a single supplier, and the loss of these manufacturers, their failure to supply us on a timely basis, or at all, or their failure to successfully carry out their contractual duties or comply with regulatory requirements, cGMP requirements, or guidance could cause delays in or disruptions to our supply chain and substantially harm our business.

We do not have any manufacturing facilities and do not expect to independently manufacture any product or product candidates. We currently rely, and expect to continue to rely, on third party manufacturers to produce all of our commercial, clinical and preclinical supply. Our reliance on third party manufacturers, who have control over the manufacturing process, increases the risk that we will not have or be able to maintain sufficient quantities of Auryxia and vadadustat or the ability to obtain such quantities at an acceptable cost or quality, which could delay, prevent or impair our and our partners' development or commercialization efforts.

We currently rely on a single source supplier for each of Auryxia drug substance and drug product and vadadustat drug substance and drug product, and alternate sources of supply may not be readily available. If any of the following occurs, we may not have sufficient quantities of Auryxia and/or vadadustat to support our clinical trials, development, commercialization, or obtaining and maintaining marketing approvals, which could materially and adversely impact our business and results of operations:

- we are unsuccessful in maintaining our current supply arrangements for commercial quantities of Auryxia and vadadustat;
- we are unsuccessful in validating new sites;
- our commercial supply arrangements for Auryxia or vadadustat are terminated;
- any of our third party manufacturers are unable to fulfill the terms of their agreements with us, including with respect to quality and quantity, or are unable or unwilling to continue to manufacture on the manufacturing lines included in our regulatory filings; or
- any of our third party manufacturers breach our supply agreements, do not comply with quality or regulatory requirements and guidance, including cGMP or are subject to regulatory review or ceases their operations for any reason.

If any of our third party manufacturers cannot or do not perform as agreed or expected, including as a result of catastrophic events, including pandemics, including the COVID-19 pandemic, terrorist attacks, wars or other armed conflicts, geopolitical tensions or natural disasters, if they misappropriate our proprietary information, if they terminate their engagements with us, if we terminate our engagements with them, or if there is a significant disagreement, 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 in a timely manner or on favorable or reasonable terms, if at all. For example, one of our manufacturers has notified us that it will be discontinuing operations at one site at a future date. 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 our current manufacturers or require us to obtain necessary regulatory approvals and licenses in order to have another third party manufacture Auryxia or vadadustat. 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 and costs associated with the qualification of a new manufacturer and validation of manufacturing processes would negatively affect our ability to supply clinical trials, obtain and maintain marketing approval, or commercialize or satisfy patient demand for Auryxia and vadadustat, where approved, in a timely manner, within budget, or at all.

In addition, the cost of obtaining Auryxia and vadadustat is subject to adjustment based on our third party manufacturers' costs of obtaining raw materials and producing the product. We have limited control over the production costs of Auryxia and vadadustat, including the costs of raw materials, and have seen increases in the production costs of Auryxia and vadadustat, and any significant increase in the cost of obtaining our products could materially adversely affect our revenue for Auryxia and vadadustat, if approved.

Moreover, issues that may arise in any scale-up and technology transfer and continued commercial scale manufacture of our products may lead to significant delays in our development, marketing approval 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. This supply interruption was resolved, and we have taken and continue to take actions designed to prevent future interruptions in the supply of Auryxia. However, we recently experienced issues in manufacturing Auryxia, and if we continue to experience manufacturing issues or our actions to prevent future interruptions are not successful, we may experience additional supply issues. In addition, before we can manufacture product at a new site, we must validate the process at that site. If the process validation is unsuccessful, or takes longer than we anticipate, we may have to expend additional resources and could experience a supply interruption. Any future supply interruptions, whether quality or quantity based, for Auryxia or vadadustat, if and where approved, would negatively and materially impact our reputation and financial condition.

There are a limited number of manufacturers that are capable of manufacturing Auryxia and vadadustat for us and complying with cGMP regulations and guidance and other stringent regulatory requirements and guidance enforced by the FDA, EMA, PMDA and other regulatory authorities. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation, which occur in addition to our own quality assurance releases. 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 vadadustat will be inspected by the FDA, the EMA and other regulatory authorities prior to or after we submit our marketing applications. Although we have general visibility into the manufacturing processes of our third party manufacturers, we do not ultimately

control such manufacturing processes of, and have little control over, our third party manufacturers, including, without limitation, their compliance with cGMP requirements and guidance for the manufacture of certain starting materials, drug substance and finished drug product. Similarly, although we review final production, we have little control over the ability of our third party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. Our third party manufacturers may experience problems with their manufacturing and distribution operations and processes, including, for example, quality issues, such as product specification and stability failures, procedural deviations, improper equipment installation or operation, utility failures, contamination, natural disasters and public health epidemics. We may also encounter difficulties relating to our own quality processes and procedures, including regulatory compliance, lot release, quality control and quality assurance, as well as shortages of qualified personnel. If our third party manufacturers cannot successfully manufacture material that conforms to our specifications and regulatory requirements and guidance, or if we or our third party manufacturers experience manufacturing, operations and/or quality issues, including an inability or unwillingness to continue manufacturing our products at all, in accordance with agreed-upon processes or on currently validated manufacturing lines, we may not be able to supply patient demand or maintain marketing approval for Auryxia, secure and maintain marketing approval for vadadustat, and we might be required to expend additional resources to obtain material from other manufacturers. If any of these events occur, our reputation and financial condition would be negatively and materially impacted. In addition, during the year ended December 31, 2022, we had higher write-downs to inventory reserves related to Auryxia drug substance that will not be forward processed into drug product. If we have additional write-downs to inventory reserves in the future, it could negatively impact our ability to supply Auryxia, and our financial condition could be harmed.

If the FDA, the EMA or other regulatory authorities do not approve the facilities being used to manufacture vadadustat, or if they withdraw any approval of the facilities being used to manufacture Auryxia or vadadustat, we may need to find alternative manufacturing facilities, which would significantly impact our ability to continue commercializing Auryxia or Vafseo in Japan, or develop, obtain marketing approval for or market vadadustat or our other product candidates, if approved.

Moreover, our failure or the failure of our third party manufacturers to comply with applicable regulations or guidance, or our failure to oversee or facilitate such compliance, could result in sanctions being imposed on us or our third party manufacturers, including, where applicable, clinical holds, fines, injunctions, civil penalties, delays in, suspension of or withdrawal of approvals, license revocation, seizures or recalls of Auryxia or Vafseo in Japan, operating restrictions, receipt of a Form 483 or warning letter, or criminal prosecutions, any of which could significantly and adversely affect the supply of Auryxia or vadadustat. For example, we previously conducted three limited, voluntary recalls of Auryxia. These and any other recalls or any supply, quality or manufacturing issues in the future and any related write-downs of inventory or other consequences could result in significant negative consequences, including reputational harm, loss of customer confidence, and a negative impact on our financials, any of which could have a material adverse effect on our business and results of operations, and may impact our ability to supply Auryxia, Vafseo in Japan or vadadustat for clinical and commercial use. Also, if our starting materials, drug substance or drug product are damaged or lost while in our or our third party manufacturers' control, it may adversely impact our ability to supply Auryxia or vadadustat, and we may incur significant financial harm.

In addition, Auryxia and vadadustat may compete with other products and product candidates for access to third party manufacturing facilities. A third party manufacturer may also encounter delays or operational issues brought on by sudden internal resource constraints, labor disputes, shifting priorities or shifting regulatory protocols including, in each case, relating to the COVID-19 pandemic. Certain of these third party manufacturing facilities may be contractually prohibited from manufacturing Auryxia or vadadustat due to exclusivity provisions in agreements with our competitors. Any of the foregoing could negatively impact our third party manufacturers' ability to meet our demand, which could adversely impact our ability to supply Auryxia or vadadustat, and we may incur significant financial harm.

Our current and anticipated future dependence on third parties for the manufacture of Auryxia and vadadustat may adversely affect our and our partners' ability to commercialize Auryxia and vadadustat, where approved, on a timely and competitive basis and may reduce any future profit margins.

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

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

- if they experience staffing difficulties;
- if we fail to communicate effectively or provide the appropriate level of oversight;

- if they undergo changes in priorities or corporate structure including as a result of a merger or acquisition or other transaction, or become financially distressed; or
- if they form relationships with other entities, some of which may be our competitors.

If the third parties upon whom we rely to conduct our trials fail to adhere to clinical trial protocols or to regulatory requirements, the quantity, quality or accuracy of the data obtained by the third parties may be compromised. We are exposed to risk of fraud or other misconduct by such third parties.

Any of these events could cause our preclinical studies 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 and maintain 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 products, any of which would adversely affect our business operations. In addition, if the third parties upon 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 development and commercialization of vadadustat, if approved, or any other product candidates.

Even though we do not directly control the third parties upon whom we rely to conduct our preclinical studies 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 and preclinical studies 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 or preclinical trial sites fail to comply with applicable GXP requirements, the clinical data generated in our 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 and preclinical 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 upon third parties to store and distribute drug product for our clinical trials. For example, we use third parties to store product at various sites in the United States to distribute to our clinical trial sites. Any performance failure on the part of our storage or distributor partners could delay clinical development, marketing approval or commercialization, resulting in additional costs and depriving us of potential product revenue.

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 all of the rights to our product, Auryxia. We have licensed and sublicensed certain rights, patent and otherwise, to Auryxia from a third party, Panion & BF Biotech, Inc., or Panion, who in turn licenses certain rights to Auryxia from one of the inventors of Auryxia. The license agreement with Panion, or the Panion License Agreement, requires us to meet development milestones and imposes development and commercialization due diligence requirements on us. In addition, under the Panion 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 the Panion 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 Panion 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 Panion 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 executed an amendment to the Panion License Agreement in accordance with the terms of the Panion Letter Agreement, following consummation of the Merger. On April 17, 2019, we and Panion entered into an amendment and restatement of the Panion License Agreement, or the Panion Amended License Agreement, which reflects certain revisions consistent with the terms of the Panion Letter Agreement. See Note 4 to our consolidated financial statements in Part I, Item 1. Financial Statements of this Quarterly Report on Form 10-Q for additional information regarding the Panion Amended License Agreement. Even though we entered into the Panion Amended License Agreement, there are no assurances that Panion will not allege other breaches of the Panion Amended License Agreement or otherwise attempt to terminate the Panion Amended 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 the Panion Amended License Agreement, 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.

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 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, which may significantly diminish our ability to exclude others from commercializing products that are similar or identical to ours. 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.

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, 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, or EPO.

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.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO 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 sooner than we expect, which would have a material adverse effect on our business.

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, in some cases, we share certain ownership and publication rights to data relating to some of our products and product candidates with research collaborators, licensees and other third parties. 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.

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

Filing, prosecuting and defending patents on our products and 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 where 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 the 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 for our products and product candidates from the intellectual property that we develop or license.

The intellectual property that we own or have licensed and related non-patent exclusivity relating to our current and future products is, and may be, limited, which could adversely affect our ability to compete in the market and adversely affect the value of Auryxia.

The patent rights and related non-patent exclusivity 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 market a product for the methods of use not 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.

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 addition to patent rights in the United States, we may seek non-patent exclusivity for vadadustat and other product candidates under other provisions of the FDCA such as new chemical entity, or NCE, exclusivity, or exclusivity for a new use or new formulation, but there is no guarantee that vadadustat or any other product candidates will receive such exclusivity. The FDCA provides a five-year period of non-patent exclusivity within the United States to the first sponsor to gain approval of an 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 sponsor does not own or have a legal right of reference to all the data required for approval.

An ANDA 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, particularly a 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 sponsor 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, a sponsor 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 sponsor.

In cases where NCE exclusivity has been granted to a new drug product, the 30-month stay triggered by such litigation is extended by the amount of time such that seven years and six months will elapse from the date of approval of the NDA for that product. Without NCE exclusivity, the 30-month stay on FDA final approval of an ANDA runs from the date on which the sponsor of the reference listed drug receives notice of a Paragraph IV certification from the ANDA sponsor.

In addition to NCE, 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.

We cannot assure you that Auryxia, vadadustat, if approved, or any of our potential future products 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 non-patent exclusivity

protection. We also cannot assure you that Auryxia, vadadustat, if approved, or any of our potential future products will obtain patent term extension.

The market entry of one or more generic competitors or any third party's attempt to challenge our intellectual property rights will likely limit Auryxia sales and have an adverse impact on our business and results of operation.

Although the composition and use of Auryxia is 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 asserting 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 potential future products. If our Orange Book-listed patents are successfully challenged by a third party and a generic version of Auryxia is approved and launched sooner than we anticipate, revenue from Auryxia could decline significantly, which would have a material adverse effect on our sales, results of operations and financial condition.

We previously received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet). We filed complaints for patent infringement relating to such ANDAs, and subsequently entered into settlement and license agreements with all such ANDA filers that allow such ANDA filers to market a generic version of Auryxia in the United States beginning on March 20, 2025. It is possible that we may receive Paragraph IV certification notice letters from additional ANDA filers and may not ultimately be successful in an ANDA litigation. For example, we received another Paragraph IV certification notice letter regarding an ANDA submitted to the FDA in February 2023 and, in March 2023, we filed a complaint for patent infringement against the ANDA filer. Generic competition for Auryxia or any of our potential future products could have a material adverse effect on our sales, results of operations and financial condition.

Litigation and administrative proceedings, including third party claims of intellectual property infringement and opposition/invalidation proceedings against third party patents, 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. Competitors may infringe our patents or misappropriate our trade secrets or confidential information. 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, third parties may have or may obtain patents in the future and claim that our products or 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, licensees or us that seeks damages or an injunction of commercial activities relating to Auryxia, vadadustat or any other product candidates or other technologies, including those that may be in-licensed or acquired, could subject us to monetary liability, a temporary or permanent injunction preventing the development, marketing and sale of such products or such technologies, and/or require our licensor, licensees or us to obtain a license to continue to develop, market or sell such products or other technologies. 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. We cannot predict whether our licensor, licensees 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. However, there may be patents of 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 product 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. 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 product and product 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. There is an increased possibility of a patent infringement claim against us with respect to commercial products. Our portfolio includes one commercial product, Auryxia. We received the CRL from the FDA

regarding our NDA for vadadustat in March 2022, and, if in the future vadadustat is approved, vadadustat could be commercialized. We attempt to ensure that our products and 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.

FibroGen has filed patent applications in the United States and other countries directed to purportedly new methods of using previously known heterocyclic carboxamide compounds for purposes of treating or affecting specified conditions, and some of these applications have since issued as patents. We have, and may in the future, initiate opposition or other legal proceedings with respect to such patents. If we are not successful in such proceedings, FibroGen could try to claim that our products infringe their patent rights. For example, we filed oppositions in the EPO, against certain of Fibrogen's patents. A number of those patents were revoked during oppositions or have since expired, but one of the patents, European Patent No 1633333, or the '333 EP Patent was maintained in restricted form. The remaining claims are directed to: treatment of anemia of chronic disease in subjects having a percent transferrin saturation of less than 20% (claim 1), treatment of anemia that is refractory to treatment with exogenously administered erythropoietin (claim 6), and treatment of iron deficiency (claim 15). We discussed the status of the opposition and/or invalidation proceedings against certain FibroGen patents in Part I, Item 3. Legal Proceedings of our Annual Report on Form 10-K for the year ended December 31, 2022.

Third parties, including FibroGen, may in the future claim that our product and product candidates and other technologies infringe upon their patents and may challenge our ability to commercialize Auryxia and vadadustat, if approved. Parties making claims against us or our licensees may seek and obtain injunctive or other equitable relief, which could effectively block our or their ability to continue to commercialize Auryxia or further develop and commercialize vadadustat or any other product candidates, including those that may be in-licensed or acquired. 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, 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 product or product candidate 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.

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 USPTO 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 USPTO or oppositions and other comparable proceedings in foreign jurisdictions. Competitors may initiate an administrative proceeding challenging our issued patents or pending patent applications, which can be expensive and time-consuming to defend. An adverse result in any current or future 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, 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 USPTO or a foreign patent office may result in substantial costs and distract our management and other employees.

We are currently involved in opposition and invalidation proceedings in the European Patent Office, Intellectual Property High Court of Japan, and the Patents Court of the UK. 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".

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.

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.

Risks Related to our Business and Managing Growth

If we fail to attract, retain and motivate senior management and qualified personnel, we may be unable to successfully develop, obtain and/or maintain marketing approval of and commercialize vadadustat or commercialize Auryxia.

Recruiting and retaining qualified 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 employees could impede the achievement of our research, development, regulatory and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Specifically, following receipt of the CRL, in April and May 2022, we implemented a reduction of our workforce by approximately 42% across all areas of our company (47% inclusive of the closing of the majority of open positions), including several members of management. In November 2022, we also implemented a reduction of our workforce, by approximately 14% consisting of individuals within our commercial organization as a result of our decision to shift to a strategic account management focused model for our commercial efforts. In addition, uncertainty related to the timing and outcome of regulatory decisions, could increase attrition. Losing members of management and other key personnel subjects us to a number of risks, including the failure to coordinate responsibilities and tasks, the necessity to create new management systems and processes, the impact on corporate culture, and the retention of historical knowledge.

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, obtain and/or maintain marketing approval of and commercialize Auryxia, vadadustat and other product candidates. Our future financial performance and our ability to develop, obtain and/or maintain marketing approval of and commercialize Auryxia and vadadustat and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to hire, train, integrate, and retain additional qualified personnel with sufficient experience. We may be unable to hire, train, retain or motivate these 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 additional members of management or other personnel leave, or we are unable to continue to attract and retain high quality personnel, our ability to grow and pursue our business strategy will be limited.

Our cost savings plan and the associated workforce reductions implemented in April, May and November 2022 may not result in anticipated savings, could result in total costs and expenses that are greater than expected and could disrupt our business.

Following receipt of the CRL, in April and May 2022, we implemented a reduction in workforce by approximately 42% across all areas of our company (47% inclusive of the closing of the majority of open positions), including several members of management. In November 2022, we also implemented a reduction of our workforce, by approximately 14% consisting of individuals within our commercial organization. The reductions in workforce reflect our strategic pillars to drive Auryxia revenue while also continuing to decrease operating costs. We may not realize, in full or in part, the anticipated benefits, savings and improvements in our cost structure from our restructuring efforts due to unforeseen difficulties, delays or unexpected costs. We recorded a restructuring charge of approximately $15.9 million and $0.1 million in the year ended December 31, 2022 and the three months ended March 31, 2023, respectively, primarily related to contractual termination benefits including severance, non-cash stock-based compensation expense, healthcare and related benefits. If we are unable to realize the expected operational efficiencies and cost savings from the restructuring, our operating results and financial condition would be adversely affected. We also cannot guarantee that we will not have to undertake additional workforce reductions or restructuring activities in the future, including as a result of the FDA's decision related to our appeal of the CRL for vadadustat. Furthermore, our cost savings plan may be disruptive to our operations, including our commercialization of Auryxia, which could affect our ability to generate product revenue. In addition, our workforce reductions could yield unanticipated consequences, such as attrition beyond planned staff reductions, or disruptions in our day-to-day operations. Our workforce reductions could also harm our ability to attract and retain qualified management, scientific, clinical, manufacturing and sales and marketing personnel who are critical to our business. Any failure to attract or retain qualified personnel could prevent us from successfully commercializing Auryxia and from successfully developing and commercializing our product candidates in the future, including vadadustat, if approved. If we are ultimately successful in obtaining approval of vadadustat in the United States, we will need to hire additional employees to support the commercialization of vadadustat in the United States, and if we are unsuccessful or delayed in doing so, the potential launch of vadadustat could be delayed.

We may encounter difficulties in managing our growth, including with respect to our employee base, and managing our operations successfully.

In our day-to-day operations, we may encounter difficulties in managing the size of our operations as well as challenges associated with managing our business. We have strategic collaborations for the commercialization of Riona and the development and commercialization of vadadustat, which is now being marketed under the trade name Vafseo™ by our collaboration partner, MTPC, in Japan. Additionally, in the United States, we have a strategic relationship with CSL Vifor related to the commercialization of vadadustat, if approved. As our operations continue, we expect that we will need to manage our current relationships and enter into new relationships, especially in light of the termination of our collaboration agreements with Otsuka, with various strategic collaborators, consultants, vendors, suppliers and other third parties. These relationships are complex and create numerous risks as we deal with issues that arise.

Our future financial performance and our ability to commercialize Auryxia and vadadustat, if and where approved, and to compete effectively will depend, in part, on our ability to manage any future growth effectively. This future growth will impose significant added responsibilities on the business and members of management. To manage any future growth, we must continue to implement and improve our managerial, operational and financial systems, procedures and processes. We may not be able to implement these improvements in an efficient or timely manner and may discover deficiencies in existing systems, procedures and processes. Moreover, the systems, procedures and processes currently in place or to be implemented may not be adequate for any such growth. Any 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 managing and, as applicable, growing our company.

In addition, we may need to further adjust the size of our workforce as a result of changes to our expectations for our business, which can result in management being required 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-related activities and related expenses. Further, we rely on independent third parties to provide certain services to us. We structure our relationships with these outside service providers in a manner that we believe results in an independent contractor relationship, not an employee relationship. If any of our service providers are later legally deemed to be employees, we could be subject to employment and tax withholding liabilities and other additional costs as well as other multiple damages and attorneys' fees.

If we fail to develop or maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, investors may lose confidence in us and the trading price of our common stock may decline.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and effectively prevent fraud and operate successfully as a public company. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If our internal control over financial reporting is not effective, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting could also restrict our future access to the capital markets.

A material weakness in internal control over financial reporting has in the past and could in the future lead to deficiencies in the preparation of financial statements. Deficiencies in the preparation of financial statements, could lead to litigation claims against us. The defense of any such claims may cause the diversion of management's attention and resources, and we may be required to pay damages if any such claims or proceedings are not resolved in our favor. Any litigation, even if resolved in our favor, could cause us to incur significant legal and other expenses. Such events could also affect our ability to raise capital to fund future business initiatives.

Security breaches and unauthorized use of our information technology systems and information, or the information technology systems or information in the possession of our collaborators and other third parties, could damage the integrity of our clinical trials, 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 cybersecurity 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 most 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 patients 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, cyberattack 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 and CCPA discussed elsewhere in these risk factors and the privacy or security rules under federal, state, or other local laws outside of the United States protecting confidential or personal information, that could be expensive to defend and could result in significant fines or other penalties. Cyberattacks 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 cyberattacks. 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.

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 adversely affected by attacks against our collaborators, vendors or service providers, and we may not have adequate contractual remedies against such collaborators, vendors and service providers to remedy any harm to our business caused by 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. 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;
- lead to public exposure of personal information of participants in our clinical trials, Auryxia patients and others;
- damage the integrity of our studies or delay their completion, disrupt our development programs, our business operations and commercialization efforts;
- compromise our ability to protect our trade secrets and proprietary information;
- damage our reputation and deter business partners from working with us; or
- divert the attention of our management and key information technology resources.

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 including the CCPA, harm our competitive position and delay the further development and commercialization of our products and product candidates, or impact our relationships with customers and patients.

Our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading. In addition, laws and regulations governing any international operations we have or may have in the future may require us to develop and implement costly compliance programs.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, CMOs, 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:

- 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. state and federal securities laws and regulations and their non-U.S. equivalents, including those related to insider trading.

We hold a marketing authorization for vadadustat from the EMA, we are seeking regulatory approval for vadadustat with countries in the ACCESS Consortium, and we conducted our global clinical trials for vadadustat, and may in the future conduct additional trials, in countries where corruption is prevalent, and 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 purpose of obtaining or keeping business or obtaining 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 SEC 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 have conducted clinical trials and in which we have CMOs 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 of 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 have conducted 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 sanction 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 commercial and clinical product and other clinical trial supplies, and for our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors ability to travel, between certain countries is subject to maintaining required licenses and complying with these laws and regulations.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state laws, and requirements of non-U.S. jurisdictions, including the GDPR. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us.

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 any future 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 Capital Market. In addition, we may incur significant costs in implementing sufficient systems, controls and processes to ensure compliance with the aforementioned laws. The laws and regulations referenced above may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements that could adversely affect our business.

Additionally, 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 known or unknown risks or preventing 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, independent contractors, CROs, CMOs, 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.

Our financial statements include goodwill and an intangible asset as a result of the Merger. The intangible asset has become impaired and could become further impaired in the future under certain conditions. In addition, goodwill could become impaired in the future under certain conditions. Any potential future impairment of goodwill or intangible assets may significantly impact our results of operations and financial condition.

As of March 31, 2023, we had approximately $118.1 million in the aggregate of goodwill and a definite lived intangible asset from the Merger. In accordance with generally accepted accounting principles, or GAAP, we are required annually, or more frequently upon certain indicators of impairment, to review our estimates and assumptions underlying the fair value of our goodwill and our definite lived intangible assets when indicators of impairment are present. Events giving rise to impairment of goodwill or intangible assets are an inherent risk in the pharmaceutical industry and often cannot be predicted.

Conditions that could indicate impairment and necessitate such a review include, but are not limited to, Auryxia's commercial performance, our inability to execute on our strategic initiatives, the deterioration of our market capitalization such that it is significantly below our net book value, a significant adverse change in legal factors, unexpected adverse business conditions,

and an adverse action or assessment by a regulator. To the extent we conclude that goodwill and/or definite lived intangible assets have become impaired, we may be required to incur material write-offs relating to such impairment and any such write-offs could have a material impact on our future operating results and financial position. For example, in the second quarter of 2020, in connection with a routine business review, we reduced our short-term and long-term Auryxia revenue forecast. This reduction was primarily driven by the impact of the September 2018 CMS decision that Auryxia would no longer be covered by Medicare for the treatment of the IDA Indication. While this decision does not impact CMS coverage for the use of Auryxia for the control of serum phosphorus levels in adult patients with CKD on dialysis, or the Hyperphosphatemia Indication, it requires all Auryxia prescriptions for Medicare patients to undergo a prior authorization to ensure their use of Auryxia for the Hyperphosphatemia Indication. As a result, we recorded an impairment charge of $115.5 million during the three months ended June 30, 2020, which was entirely allocated to our only intangible asset, the developed product rights for Auryxia, and made a corresponding adjustment to the estimated useful life of the developed product rights for Auryxia, which we again adjusted during the three months ended December 31, 2020. The estimates, judgments and assumptions used in our impairment testing, and the results of our testing, are discussed in Note 8 to our consolidated financial statements in Part I, Item 1. Financial Statements of this Quarterly Report on Form 10-Q. If these estimates, judgments and assumptions change in the future, including if the Auryxia asset group does not meet its current forecasted projections, additional impairment charges related to goodwill or our intangible asset could be recorded in the future and additional corresponding adjustments may need to be made to the estimated useful life of the developed product rights for Auryxia, which could materially impact our financial position, certain of our material agreements, and our future operating results.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of Auryxia or vadadustat, if approved.

We face an inherent risk of product liability as a result of the clinical and commercial use of Auryxia and vadadustat. For example, we may be sued if Auryxia or vadadustat allegedly causes injury or is found to be otherwise unsuitable during clinical trials, 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 Auryxia or vadadustat, if approved. 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 Auryxia or vadadustat, if approved;
- 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 Auryxia or vadadustat;
- 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 Auryxia or vadadustat, if approved;
- loss of revenue;
- the inability to commercialize Auryxia or vadadustat, if approved; 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 additional product liability risks that may arise. Consequently, a product liability claim may result in losses that could be material to our business.

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, we operate in a demanding regulatory environment, and we have and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Capital 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 certain corporate governance practices. In particular, our compliance with Section 404 of the Sarbanes-Oxley Act has required and will continue to require that we incur substantial accounting-related expenses and expend significant management efforts. Our testing, or the testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls that we would be required to remediate in a timely manner. If we are not able to comply with the requirements of the Sarbanes-Oxley Act, we could be subject to sanctions or investigations by the SEC, the Nasdaq Capital Market or other regulatory authorities, which would require additional financial and management resources and could adversely affect the market price of our securities. Furthermore, if we cannot provide reliable financial reports or prevent fraud, including as a result of remote working by our employees, our business and results of operations would likely be materially and adversely affected.

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.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our Ninth Amended and Restated Certificate of Incorporation, as amended, or Charter, and our Amended and Restated By-Laws, or Bylaws, as amended to date, contain provisions that eliminate, to the maximum extent permitted by the General Corporation Law of the State of Delaware, or DGCL, the personal liability of our directors and executive officers for monetary damages for breach of their fiduciary duties as a director or officer. Our Charter and our Bylaws also provide that we will indemnify our directors and executive officers and may indemnify our employees and other agents to the fullest extent permitted by the DGCL.

In addition, as permitted by Section 145 of the DGCL our Bylaws and our indemnification agreements that we have entered into with our directors and executive officers provide that:

- We will indemnify our directors and officers, as defined in our Bylaws, for serving us in those capacities or for serving other related business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of Akebia and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- The rights conferred in our Bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.

Any claims for indemnification made by our directors or officers could impact our cash resources and our ability to fund the business.

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

Under Section 382 of the Internal Revenue Code, or Section 382, 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 an ownership change under Section 382. In addition, the Tax Cuts and Jobs Act, including amendments made by the CARES Act, includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to fully offset taxable income in the future. 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 generate 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. At the state level, state net operating losses generated in one state cannot be used to offset income generated in another state and 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, Need for Additional Capital and Growth Strategy," 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. taxable income necessary to utilize our NOLs.

Our Charter designates the Court of Chancery of 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 Charter provides that, subject to limited exceptions, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) 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, (iii) any action asserting a claim against us arising pursuant to any provision of the DGCL our Charter or our Bylaws, or (iv) any other action asserting a claim against us, our directors, officers or other employees that is governed by the internal affairs doctrine. Under our Charter, 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 Charter 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 Charter 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 legal proceedings that could result in substantial costs and divert management's attention, and we could be subject to additional legal proceedings.

We are currently subject to legal proceedings, including those described in Part II, Item 1. Legal Proceedings in this Quarterly Report on Form 10-Q, and additional claims may arise in the future. 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 Quarterly Report on Form 10-Q following a decline in the market price of their securities. For example, we were party to a putative class action lawsuit in state court filed by purported Keryx stockholders challenging the disclosures made in connection with the Merger, including those that relate to vadadustat's safety, approvability and commercial viability. Oral argument was held on October 7, 2022, and the Court dismissed the complaint without prejudice on October 17, 2022, giving plaintiffs thirty days to amend their complaint. On November 16, 2022, plaintiffs filed an amended consolidated complaint, asserting the same claims and seeking the same relief as the consolidated complaint. On January 18, 2023, defendants moved to dismiss the amended consolidated complaint in its entirety. Briefing on defendants' motion to dismiss the amended consolidated complaint was completed on April 5, 2023 and oral argument is currently scheduled to be held on June 21, 2023. 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. Monetary damages or any other adverse judgment would have a material adverse effect on our business and financial position. In addition, if other resolution or actions taken as a result of legal proceedings were to restrain our ability to operate or market our products and services, our consolidated financial position, results of operations or cash flows could be materially adversely affected. We could also suffer an adverse impact on our reputation, negative publicity and a diversion of management's attention and resources, which could have a material adverse effect on our business.

Risks Related to our Common Stock

Our stock price has been and may continue to be volatile, which could result in substantial losses for holders or future 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 similarly situated biopharmaceutical companies specifically 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 Stock Market has ranged from a low of $0.24 on October 24, 2022 to a high of $31.00 on June 20, 2014. The daily closing market price for our common stock varied between a high price of $1.15 on February 8, 2023 and a low price of $0.56 on March 31, 2023 in the three-month period ended March 31, 2023. During that time, the price of our common stock ranged from an intra-day low of $0.54 per share to an intra-day high of $1.20 per share. 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, including, among others, developments related to and results of our research or clinical trials, developments related to our regulatory submissions and meetings with regulatory authorities, in particular as it relates to vadadustat, commercialization of Auryxia, vadadustat in Europe and, if and as approved in the U.S. and foreign markets, and any other product candidates, announcements by us or our competitors of significant transactions or strategic collaborations, negative publicity around Auryxia or vadadustat, regulatory or legal developments in the United States and other countries, developments or disputes concerning our intellectual property, the recruitment or departure of key personnel including as a result of our reductions in workforce, actual or anticipated changes in estimates as to financial results, changes in the structure of healthcare payment systems, market conditions in the biopharmaceutical sector, potential delisting from The Nasdaq Stock Market and other factors beyond our control. As a result of this volatility, our stockholders 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 II, Item 1. Legal Proceedings of this Quarterly Report on Form 10-Q for information concerning securities class action initiated against 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 stockholders will dilute our stockholders' 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.

As of March 31, 2023 and based on the amounts reported in the most recent filings made under Section 13(d) and 13(g) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, Muneer A. Satter, or Satter, beneficially owned approximately 8.1% of our outstanding shares of common stock, the Vanguard Group, or Vanguard, beneficially owned approximately 6.0% of our outstanding shares of common stock, and CSL Vifor beneficially owned approximately 4.1% of our outstanding shares of common stock. By selling a large number of shares of common stock, Satter or Vanguard could cause the price of our common stock to decline. The shares beneficially owned by CSL Vifor 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, but if they are registered in the future, those shares would become freely tradable and, if a large portion of such shares are sold, could cause the price of our common stock to decline.

We have a significant number of shares that are subject to outstanding options and restricted stock units, and in the future we may issue additional options, restricted stock units, or other derivative securities convertible into our common stock. The exercise or vesting of any such options, restricted stock units, 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. 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 a shelf registration statement, which allows us to offer and sell up to $300 million in registered securities, such as common stock, preferred stock, debt securities, 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, including a sales agreement prospectus that covers the offering, issuance and sale by us of up to a maximum aggregate offering price of up to $26 million of our common stock that may be issued and sold from time to time under a sales agreement with Jefferies LLC.

Sales of substantial amounts of shares of our common stock or other securities by our employees or our other stockholders or by us under our shelf registration statement, pursuant to at-the-market offerings 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.

Our executive officers, directors and principal stockholders maintain the ability to significantly influence all matters submitted to stockholders for approval.

As of March 31, 2023, our executive officers, directors and principal stockholders, in the aggregate, beneficially owned shares representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

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 Charter and our Bylaws 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 Bylaws; 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 Charter.

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 DGCL 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.

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 and we currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. Any payment of cash dividends in the future would be at the discretion of our Board of Directors and would depend on, among other things, our earnings, financial condition, capital requirements, level of indebtedness, statutory and contractual restrictions applying to the payment of dividends and other considerations that the Board of Directors deems relevant. In addition, the terms of the Loan Agreement preclude us from paying cash dividends and future debt agreements may preclude us from paying cash 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 2. Unregistered Sales of Equity Securities and Use of Proceeds.

Sales of Unregistered Securities

During the quarter ended March 31, 2023, we did not have any sales of unregistered securities.

Item 3. Defaults Upon Senior Securities.

Not applicable.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

As previously disclosed, on May 9, 2022, in connection with our workforce reduction, we entered into a retention and separation agreement with each of Michel Dahan, our Chief Operating Officer, and Nicole Hadas, our Chief Legal Officer. Pursuant to the retention and separation agreements as amended on November 2, 2022, each of Mr. Dahan and Ms. Hadas would separate from the Company effective as of May 5, 2023, or, in the event of certain specified events, the effective date of their separation would extend to October 20, 2023.

On May 3, 2023, the Compensation Committee of the Board of Directors of the Company approved amendments to Mr. Dahan's and Ms. Hadas's separation agreements to, among other things, extend the termination effective date for Mr. Dahan and Ms. Hadas. Specifically, the amendments extend the termination effective date for Mr. Dahan and Ms. Hadas to July 28, 2023 and, in the event of certain specified events, the effective date of each of their terminations may be extended up to January 26, 2024. The amendments also increase Mr. Dahan's and Ms. Hadas's opportunity to earn cash bonuses under our Cash Incentive Plan upon the achieve of certain milestones from $150,000 to $300,000 in the case of Mr. Dahan and from $150,000 to $250,000 in the case of Ms. Hadas. In addition, Mr. Dahan and Ms. Hadas will each receive, on May 12, 2023, an additional restricted stock unit, or RSU, grant for 200,000 shares of common stock and 100,000 shares of common stock, respectively. The RSUs will vest as to one third (1/3) of the shares on each of the first, second and third anniversaries of the grant date, subject to the executive officers' continued service with the Company through each such date, and will accelerate in connection with a change in control of the Company.

Item 6. Exhibits.

Exhibits

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	Certificate of Amendment of Ninth Amended and Restated Certificate of Incorporation of Akebia Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on June 9, 2020).
3.3	Second Amended and Restated Bylaws (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on April 28, 2023).
10.1*	Amended and Restated Non-Employee Director Compensation Program, effective April 27, 2023.
10.2*#	Amendment No. 5 to Master Manufacturing Services and Supply Agreement, dated February 28, 2023, by and between Keryx Biopharmaceuticals, Inc. and Siegfried Evionnaz SA.
10.3*†	Form of Stock Appreciation Rights Award Agreement for officers.
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.
101.INS*	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document)
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Labels Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

* Filed, or submitted electronically, herewith
# Indicates portions of the exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K
† Indicates management contract or compensatory plan.

SIGNATURES

Pursuant to the requirements 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: May 8, 2023

By: /s/ John P. Butler

John P. Butler

President and Chief Executive Officer (Principal Executive Officer)

Date: May 8, 2023

By: /s/ David A. Spellman

David A. Spellman

Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)

AKEBIA THERAPEUTICS, INC.
AMENDED AND RESTATED NON-EMPLOYEE DIRECTOR COMPENSATION PROGRAM

Effective April 27, 2023

Non-employee members of the Board of Directors (the "***Board***") of Akebia Therapeutics, Inc. (the "***Company***") shall be eligible to receive cash and equity compensation as set forth in this Non-Employee Director Compensation Program (this "***Program***"). The cash and equity compensation described in this Program shall be paid or be made, as applicable, automatically and without further action of the Board, to each member of the Board who is not an employee of the Company or any parent or subsidiary of the Company (each, a "***Non-Employee Director***") who is eligible to receive such cash or equity compensation, unless such Non-Employee Director declines the receipt of such cash or equity compensation by written notice to the Company. This Program shall remain in effect until it is revised or rescinded by further action of the Board. This Program shall be reviewed by the Board periodically and may be amended, modified or terminated by the Board at any time in its sole discretion and nothing herein should be construed as a guarantee to any Non-Employee Director of any particular level of cash or equity compensation. The terms and conditions of this Program shall supersede any prior cash and/or equity compensation arrangements for service as a member of the Board between the Company and any of its Non-Employee Directors. This Program shall become effective on the date set forth above (the "***Effective Date***").

1. Cash Compensation.

(a) Annual Retainers. Each Non-Employee Director shall be eligible to receive an annual retainer of $45,000 for service on the Board.

(b) Additional Annual Retainers. In addition to the annual retainer payable pursuant to Section 1(a) above, a Non-Employee Director shall be eligible to receive the following annual retainers:

(i) Chairperson of the Board. A Non-Employee Director serving as Chairperson of the Board shall be eligible to receive an additional annual retainer of $35,000 for such service; provided, that, in the event that a Non-Employee Director is one of two concurrently serving Chairpersons of the Board, the additional annual retainer payable to such Non-Employee Director pursuant to this Section 1(b)(i) shall be $17,500.

(ii) Audit Committee. A Non-Employee Director serving as Chairperson of the Audit Committee of the Board (the "***Audit Committee***") shall be eligible to receive an additional annual retainer of $20,000 for such service. A Non-Employee Director serving as a member of the Audit Committee (other than the Chairperson of the Audit Committee) shall be eligible to receive an additional annual retainer of $10,000 for such service.

(iii) Compensation Committee. A Non-Employee Director serving as Chairperson of the Compensation Committee of the Board (the "***Compensation Committee***") shall be eligible to receive an additional annual retainer of $15,000 for such service. A Non-Employee Director serving as a member of the Compensation Committee (other than the Chairperson of the Compensation Committee) shall be eligible to receive an additional annual retainer of $7,500 for such service.

(iv) Nominating and Corporate Governance Committee. A Non-Employee Director serving as Chairperson of the Nominating and Corporate Governance Committee of the Board (the "***NCG Committee***") shall be eligible to receive an additional annual retainer of $10,000 for such service. A Non-Employee Director serving as a member of the NCG Committee (other than the Chairperson of the NCG Committee) shall be eligible to receive an additional annual retainer of $5,000 for such service.

(v) Research and Development Committee. A Non-Employee Director serving as Chairperson of the Research and Development Committee of the Board (the "***R&D Committee***") shall be eligible to receive an additional annual retainer of $10,000 for such service. A Non-Employee Director serving as a member of the R&D Committee (other than the Chairperson of the R&D Committee) shall be eligible to receive an additional annual retainer of $5,000 for such service.

(c) Payment of Retainers. The annual retainers described in Sections 1(a) and 1(b) shall be earned on a quarterly basis based on a calendar quarter and shall be paid in cash by the Company in arrears not later than the fifteenth day following the end of each calendar quarter. In the event a Non-Employee Director does not serve as a Non-Employee Director, or in the applicable positions described in Section 1(b), for an entire calendar quarter, the retainer paid to such Non-Employee Director shall be prorated for the portion of such calendar quarter actually served as a Non-Employee Director, or in such position, as applicable.

2. Equity Compensation. Non-Employee Directors shall be granted the equity awards described below. Each award described below shall be granted under and shall be subject to the terms and provisions of the Company's 2014 Incentive Plan, as amended, or any other successor Company equity incentive plan under which awards are permitted to be made to Non-Employee Directors (the "***Equity Plan***") and (i) for option awards, a non-qualified stock option award agreement, including attached exhibits, in substantially the form of award agreement applicable to Non-Employee Directors most recently approved by the Board and/or the Compensation Committee, as applicable, and (ii) for restricted stock unit awards, a restricted stock unit award agreement, including attached exhibits, in substantially the form of award agreement applicable to Non-Employee Directors most recently approved by the Board and/or the Compensation Committee, as applicable. All applicable terms of the Equity Plan apply to this Program as if fully set forth herein. For the avoidance of doubt, if there is any conflict between the terms of the Equity Plan (including the applicable award agreements thereunder) and this Program, the Equity Plan (including the applicable award agreements thereunder) shall control.

(a) Initial Awards. Each Non-Employee Director who is initially elected or appointed to the Board after the Effective Date shall be eligible to receive, on the date of such initial election or appointment, an option to purchase 180,000 shares of the Company's common stock (subject to adjustment as provided in the Equity Plan). The awards described in this Section 2(a) shall be referred to as "***Initial Awards***." No Non-Employee Director shall be granted more than one Initial Award.

(b) Subsequent Awards. A Non-Employee Director who (i) has been serving on the Board for at least six months as of the date of any annual meeting of the Company's stockholders after the Effective Date and (ii) will continue to serve as a Non-Employee Director immediately following such meeting, shall be automatically granted, on the date of such annual meeting, an option to purchase 45,000 shares of the Company's common stock (subject to adjustment as provided in the Equity Plan) and 30,000 restricted stock units of the Company. The option awards described in this Section 2(b) shall be referred to as "***Subsequent Options***", the restricted stock unit awards described in this Section 2(b) shall be referred to as "***Subsequent RSUs***", and the Subsequent Options and Subsequent RSUs shall together be referred to as the "***Subsequent Awards***." For the avoidance of doubt, a Non-Employee Director

elected for the first time to the Board at an annual meeting of the Company's stockholders shall only receive an Initial Award in connection with such election, and shall not receive any Subsequent Awards on the date of such meeting as well.

(c) Termination of Service of Employee Directors. Members of the Board who are employees of the Company or any parent or subsidiary of the Company who subsequently terminate their service with the Company and any parent or subsidiary of the Company and remain on the Board will not receive an Initial Award pursuant to Section 2(a) above, but to the extent that they are otherwise eligible, will be eligible to receive, after termination from service with the Company and any parent or subsidiary of the Company, Subsequent Awards as described in Section 2(b) above.

(d) Terms of Awards Granted to Non-Employee Directors.

(i) Purchase Price. The per share exercise price of each option granted to a Non-Employee Director shall equal the fair market value (as determined pursuant to the Equity Plan) of a share of the Company's common stock on the date the option is granted.

(ii) Vesting. Each Initial Award shall vest and become exercisable in accordance with the following schedule, subject to the Non-Employee Director remaining in continuous employment or other service relationship with the Company ("***Service***") through each such vesting date: 33 1/3% of the Initial Award shall vest on the one-year anniversary of the date of grant and 66 2/3% shall vest ratably on the first day of each calendar quarter between the one-year anniversary of the date of grant and the third anniversary of the date of grant. Each Subsequent Option shall vest and become exercisable in full on the first anniversary of the date of grant (or, if earlier, immediately prior to the first annual meeting of the Company's stockholders occurring after the date of grant), subject to the Non-Employee Director remaining in continuous Service through such vesting date. Each Subsequent RSU shall vest in full on the first anniversary of the date of grant subject to the Non-Employee Director remaining in continuous Service through such vesting date. Each Initial Award and Subsequent Option that is then-outstanding shall vest and become exercisable in full upon a change in control of the Company or termination of the Non-Employee Director's Service due to the Non-Employee Director's death or Disability. For purposes of the Program, "***Disability***" means Executive's inability by reason of physical or mental impairment to perform his/her job duties for a period exceeding twelve (12) consecutive weeks.

(iii) Term. The term of each option granted to a Non-Employee Director shall be ten (10) years from the date the option is granted.

3. Non-Employee Director Compensation Limit. Notwithstanding anything herein to the contrary, the cash compensation and equity compensation that each Non-Employee Director is entitled to receive under this Program shall be subject to any limits set forth in the applicable Equity Plan with respect to limits on awards to Non-Employee Directors.

4. Reimbursements. The Company shall reimburse each Non-Employee Director for all reasonable, documented, out-of-pocket travel and other business expenses incurred by such Non-Employee Director in the performance of such Non-Employee Director's duties to the Company in accordance with the Company's applicable expense reimbursement policies and procedures, as in effect from time to time. To the extent that any reimbursement under this Program provides for a deferral of compensation under Section 409A of the Internal Revenue Code of 1986, as amended: (a) the amount eligible for reimbursement in one calendar year may not affect the amount eligible for reimbursement in any other calendar year; (b) the right to reimbursement is not subject to liquidation or exchange for another benefit; and (c) any such

reimbursement of an expense must be made on or before the last day of the calendar year following the calendar year in which the expense was incurred.

Exhibit 10.2

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential.
Double asterisks denote omissions.

AMENDMENT NO. 5 TO
MASTER MANUFACTURING SERVICES AND SUPPLY AGREEMENT

This Amendment No. 5 to Master Manufacturing Services and Supply Agreement ("Amendment No. 5") is made effective and entered into on February 28, 2023 (the "Amendment No. 5 Effective Date") by and between **Siegfried Evionnaz SA**, with principal offices located at Route du Simplon 1, 36, 1902 Evionnaz, Switzerland (together with its Affiliates and subsidiaries "Vendor"); and **Keryx Biopharmaceuticals, Inc.**, with its offices at 245 First Street, Cambridge, Massachusetts, USA 02142 ("Keryx").

WHEREAS, Vendor and Keryx entered into a Master Manufacturing Services and Supply Agreement dated December 20, 2017, as amended ("Agreement") under which Vendor manufactures Product for purchase by Keryx; and

WHEREAS, on December 12, 2018, Keryx merged with Akebia Therapeutics, Inc. ("Akebia") and, pursuant to such merger, Akebia assumed all of Keryx's rights and obligations under the Agreement. Keryx continues to operate as a wholly owned subsidiary of Akebia, and Akebia is an Affiliate of Keryx; and

WHEREAS, the Parties wish to amend the Agreement as herein provided;

NOW THEREFORE, the Parties hereto mutually agree as follows:

1. For the purpose of this Amendment No. 5, the defined terms used herein shall have the same meanings as those used in the Agreement, unless otherwise specified in this Amendment No. 5.

2. Effective as of the Amendment No. 5 Effective Date, new sections 3.4.4, 3.4.5, 3.17 and 3.18 are hereby added to the Agreement and section 3.5 is revised as follows:

   3.4.4 no later than [**], for [**], upon receipt of which Vendor shall within [**] confirm its acceptance in writing and, in accordance with Section 3.8, provide a delivery schedule mutually acceptable for both Parties that sets out delivery dates for specified quantities of Product.

   3.4.5 subject to Keryx election to extend the Term through [**] as outlined under section 16.1.1: no later than [**], for [**], upon receipt of which Vendor shall within [**] confirm its acceptance in writing and, in accordance with Section 3.8, shall provide a delivery schedule that sets out delivery dates for specified quantities of Product.

   3.5 Keryx will have the obligation to purchase minimum annual quantities of the Product at the Product Price, as set forth in Attachment B, during the Term of the Agreement. [**] Minimum Annual Purchase Obligation [**] and the Product Price are set forth in Attachment B. In the event that Vendor is [**] for the delivery of Product pursuant to a binding Order for a given calendar year during the Term [**], Vendor shall provide a regular [**] updated production schedule ("Updated Schedule") [**].

   3.17 The Order BPA 114 placed by Keryx for [**] of Product out of [**] Manufacturing Facility remains valid. Vendor shall use commercially reasonable efforts to deliver the Order BPA 114 no later than [**]. However, in the event the delivery of the Product ordered under BPA 114 is not complete by the above-mentioned date, the remaining Product shall be delivered by Vendor no later than [**], provided that manufacture of Product at [**] Manufacturing Facility takes place continuously.

   3.18 The Parties agree that the Batches manufactured from the [**] Manufacturing Facility as set out in Exhibit 3 hereto (out of the Reprocessing Validation Campaign) are to be sold by Vendor and purchased by Keryx at a Product Price of EUR [**], on the condition that [**].

3. Effective as of the Amendment No. 5 Effective Date, section 6.1.3 shall be deleted and replaced by the following:

6.1.3 For each Batch, Vendor will release Product against the Specifications and make available to Keryx a complete and accurate copy of the Batch records, containing all of the documentation and information set forth in Attachment F (collectively, the "Batch Documentation") for such Batch ("Vendor Product Release"). Pursuant to Exhibit 4, a procedure that has been agreed between the parties and summarized under Exhibit 4, attached hereto, after the first [**] Batches of Product have been Manufactured by Vendor in a calendar year, and in accordance with the associated criteria detailed in Exhibit 4, Keryx shall move from a full review of the Batch Documentation to a reduced review of the Batch Documentation. Notwithstanding the foregoing, also in accordance with Exhibit 4, Keryx may revert their review of the Batch Documentation back to a full review, based on the criteria detailed in Exhibit 4.

Keryx will respond within [**] to Vendor after notice of Vendor Product Release and will provide Vendor with either (i) an authorization to deliver form or (ii) notification of rejection for non-compliance with the Specifications. If Keryx has determined that the Batch does not comply with the Specifications, the Parties shall proceed according to Sections 6.1.23 and 6.1.24 herein. Upon reasonable request, Vendor will also deliver to Keryx all Manufacturing Records, and other supporting documentation in the possession or under the control of Vendor relating to the manufacture of each Batch of Product (or any intermediate or component of Product).

If Vendor has provided the requisite documentation specified in this Section 6.1.3 and Keryx has not responded within [**], the Batch shall be deemed authorized to be delivered to Keryx, provided that Keryx still retains its rights of rejection as specified in Section 6.1.22. Keryx will use reasonable efforts to collect such Product for shipment as provided for in Section 3.10 herein within [**]. Any scope changes to the release requirements or quality requirements and associated impact(s), including impacts to costs, will be reviewed and assessed prior to implementation, and in all cases subject to the prior written approval of Keryx.

4. Effective as of the Amendment No. 5 Effective Date, the text of Section 16.1.1 shall be deleted and replaced by the following:

16.1 **Term.**

16.1.1 The term of this Agreement (the "Term") shall commence as of the Agreement Date and, subject to earlier termination in accordance with the provisions of this Section 16, shall end on December 31, 2024 unless otherwise agreed by the Parties. Notwithstanding the foregoing, Keryx may elect to extend the Term through December 31, 2026 with written notice sent at least twelve (12) months prior to the expiry of the Term, in accordance with Section 22 herein. In the event of such an election by Keryx, Keryx's Minimum Annual Purchase Obligation for [**] through [**] set forth in **Attachment B** shall apply. For the avoidance of doubt, expiration of the Term in accordance with this Section 16.1.1 shall not relieve Keryx of its responsibilities to pay any undisputed invoices issued by Vendor for Product or other Services performed in accordance with Section 3 of the Agreement.

5. Effective as of the Amendment No. 5 Effective Date, Section 16.8 of the Agreement shall be deleted and replaced by the following:

16.8 Reinstatement of [**] Manufacturing Facility.

16.8.1 Notwithstanding any other term in the Agreement, upon the Amendment No. 5 Effective Date, the [**] Facility is hereby reinstated as a Manufacturing Facility under the Agreement. At such time, Keryx's Minimum Annual Purchase Obligation, Keryx's Forecasting obligations, Vendor's Operational Capacity obligations and other obligations of Vendor and Keryx under this Agreement shall apply also to the [**] Facility.

6. Effective as of the Amendment No. 5 Effective Date, Section 16.9 is hereby added to the Agreement:

16.9 **Removal of [**] Manufacturing Facility.**

16.9.1 Notwithstanding any other term in the Agreement, including the Minimum Annual Purchase Obligation detailed in Attachment B, as of [**] (as such date may be extended in accordance with Section 16.8.2, the "[**] Removal Date"), the [**] Manufacturing Facility will be removed as a Manufacturing Facility under this Agreement. Removal of the [**] Manufacturing Facility pursuant to this Section 16.8.1 shall, as of the [**] Removal Date, eliminate Keryx's Minimum Annual Purchase Obligation, Keryx's Forecasting obligations, Vendor's Operational Capacity obligations and other obligations of Vendor under this Agreement associated with the [**] Manufacturing Facility (except (i) Vendor's obligation to maintain any Product on stability studies and (ii) any obligations that are arising out of provisions deemed to survive the expiration or termination of this Agreement as set forth under Section 16.7 of this Agreement), and shall render the [**] Manufacturing Facility as [**] under this Agreement. For the avoidance of doubt, the foregoing removal of the [**] Manufacturing Facility as a Manufacturing Facility under this Agreement shall not relieve Keryx of its responsibilities to pay any undisputed invoices issued by Vendor for Product or other Services performed, in accordance with Section 3 of the Agreement.

7. Effective as of the Amendment No. 5 Effective Date, **Attachment A** (Expansion Services and Operational Capacity) of the Agreement is hereby deleted in its entirety and replaced with the text of Exhibit 1 hereto.

8. Effective as of the Amendment No. 5 Effective Date, the text of **Attachment B** (Product Price) of the Agreement is hereby deleted in its entirety and replaced with the text of Exhibit 2 hereto.

9. From and after this Amendment No. 5 Effective Date, all references in the Agreement to "this Agreement," "hereof," "herein," and similar words or phrases shall mean and refer to the Agreement as amended by this Amendment No. 5.

10. Except as provided for in this Amendment No. 5, all other terms and conditions of the Agreement shall remain in full force and effect.

11. The governing law and jurisdiction applicable to the Agreement shall apply to this Amendment No. 5.

[Signature Page to Follow]

IN WITNESS WHEREOF, the Parties hereto have caused this Amendment No. 5 to be executed by their duly authorized representatives as of the date first above written.

Signed on behalf of Siegfried Evionnaz SA

By: /s/ Marianne Spane
Name: Marianne Spane, CBO

Date: Feb 27 2023

Signed on behalf of Keryx Biopharmaceuticals, Inc.

By: /s/ David Spellman
Name: David Spellman, Authorized Signatory,
Chief Financial Officer, Akebia Therapeutics, Inc.

Date: Feb 28 2023

Signed on behalf of Siegfried Evionnaz SA

By: /s/ Marcel Signer
Name: Marcel Signer, Site Manager

Date: Feb 27 2023

Signed on behalf of Keryx Biopharmaceuticals, Inc.

By: /s/ John Butler
Name: John Butler, Authorized Signatory,
Chief Executive Officer, Akebia Therapeutics, Inc.

Date: Feb 28 2023

EXHIBIT 2

ATTACHMENT B – PRODUCT PRICE AND MINIMUM ANNUAL PURCHASE OBLIGATION

	[**]		**[**]**	
[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	
[**]	[**]		[**]	[**]
[**]	[**]		[**]	[**]

[**]

Name:	[—]
Number of Shares of Stock subject to SAR:	[—]
Base Value Per Share:	$[—]
Date of Grant:	[—]

OFFICER STOCK APPRECIATION RIGHTS AWARD

granted under the

AKEBIA THERAPEUTICS, INC.
2014 INCENTIVE PLAN

STOCK APPRECIATION RIGHTS AGREEMENT

This agreement (the "Agreement") evidences a SAR granted by Akebia Therapeutics, Inc. (the "Company") to the undersigned (the "Grantee"), pursuant to and subject to the terms of the Akebia Therapeutics, Inc. 2014 Incentive Plan, as amended (the "Plan").

1. Grant of SAR. The Company grants to the Grantee on the date set forth above (the "Date of Grant") a SAR Award (the "SAR"), on the terms provided herein and in the Plan, with respect to the number of shares of Stock of the Company set forth above (the "Shares") at a base value per Share as set forth above, in each case subject to adjustment pursuant to Section 7 of the Plan in respect of transactions occurring after the date hereof.

2. Meaning of Certain Terms. Except as otherwise defined herein, all capitalized terms used herein have the same meaning as in the Plan. The following terms have the following meanings:

(a) "Beneficiary" means, in the event of the Grantee's death, the beneficiary named in the written designation (in form acceptable to the Administrator) most recently filed with the Administrator by the Grantee prior to the Grantee's death and not subsequently revoked, or, if there is no such designated beneficiary, the executor or administrator of the Grantee's estate. An effective beneficiary designation will be treated as having been revoked only upon receipt by the Administrator, prior to the Grantee's death, of an instrument of revocation in form acceptable to the Administrator.

(b) "Change in Control" means the occurrence of any of the following events other than in connection with the consummation of an initial public offering of the Company's securities: (i) any "person" (as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended) who is not a shareholder of the Company as of the date of this Agreement or an affiliate thereof is or becomes the "beneficial owner" (as defined in Rule 13d-3 under said Act), directly or indirectly, of securities of the Company representing 50% or more of the total voting power represented by the Company's then outstanding voting securities; (ii) a change in the composition of the Board occurring within a two-year period, as a result of which less than a majority of the directors are Incumbent Directors; (iii) the date of the consummation of a merger, scheme of arrangement or consolidation of the Company with any other corporation that has been approved by the stockholders of the Company, other than a merger, scheme of arrangement or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity) more than fifty percent (50%) of the total voting power represented by the voting securities of the Company or such surviving entity outstanding immediately after such merger or consolidation; or (iv) the date of the consummation of the sale or disposition by the Company of all or substantially all the Company's assets. Notwithstanding the foregoing, a transaction will not constitute a Change in Control if: (i) its sole purpose is to change the domicile of the Company's incorporation; or (ii) its sole purpose is to create a holding company that will be owned in substantially the same proportions by the persons who held the Company's securities immediately before such transaction. In all respects, the definition of Change in Control shall be interpreted to comply with Section 409A of the Code, and any successor statute, regulation and guidance thereto.

(c) "Incumbent Directors" means directors who either (A) are directors of the Company as of the date hereof, or (B) are elected, or nominated for election, to the Board with the affirmative votes of at least a majority of the remaining Incumbent Directors at the time of such election or nomination (but will not include an individual whose election or nomination is in connection with an actual or threatened proxy contest relating to the election of directors to the Company).

(d) "SAR Holder" means the Grantee or, if as of the relevant time the SAR has passed to a Beneficiary, the Beneficiary.

3. Vesting; Method of Exercise; Treatment of the SAR Upon Cessation of Employment and a Change in Control.

(a) Vesting. As used herein with respect to the SAR or any portion thereof, the term "vest" means to become exercisable and the term "vested" as applied to any outstanding SAR means that the SAR is then exercisable, subject in each case to the terms of the Plan. Unless earlier terminated, forfeited, relinquished or expired, and subject to the immediately following sentence and the terms of any Executive Severance Agreement or other written agreement between the Grantee and the Company, the SAR will vest in accordance with the terms of Schedule A attached hereto. Notwithstanding the foregoing, the SAR, to the extent outstanding immediately prior to a Change in Control but not then vested in full, shall automatically and immediately become fully vested and exercisable upon such Change in Control.

(b) Exercise of the SAR. No portion of the SAR may be exercised until such portion vests. Exercise of the SAR shall entitle the Grantee to a number of Shares with a fair market value equal to (i) the difference between (x) the fair market value of one Share as of the date of exercise and (y) the base value per Share of the SAR, multiplied by (ii) the number of Shares with respect to which this SAR is being exercised; provided, that, no fractional Shares will be delivered hereunder and if the application of the foregoing formula would result in a fractional Share, the number of Shares issues upon exercise of the SAR shall be rounded down to the nearest whole share. The Company shall deliver such Shares, subject to satisfaction by the Grantee of any applicable tax withholding obligations pursuant to Section 6 hereof, as soon as administratively possible and, in any event, within thirty (30) days following the date of exercise.

Each election to exercise any vested portion of the SAR will be subject to the terms and conditions of the Plan and shall be in writing and signed by the SAR Holder (or in such other form as is acceptable to the Administrator). Each such written exercise election must be received by the Company at its principal office or by such other party as the Administrator may prescribe. In the event that the SAR is exercised by a person other than the Grantee, the Company will be under no obligation to deliver Shares hereunder unless and until it is satisfied as to the authority of the SAR Holder to exercise the SAR and compliance with applicable securities laws. The latest date on which the SAR or any portion thereof may be exercised will be the 10th anniversary of the Date of Grant (the "Final Exercise Date"). If the SAR is not exercised by the Final Exercise Date the SAR or any remaining portion thereof will thereupon immediately terminate.

(c) Treatment of the SAR Upon Cessation of Employment. If the Grantee's Employment ceases, the SAR, to the extent not already vested, will be immediately forfeited, and any vested portion of the SAR that is then outstanding will be treated as follows:

(i) Subject to clauses (ii) and (iii) below and Section 4 of this Agreement, the SAR to the extent vested immediately prior to the cessation of the Grantee's Employment will remain exercisable until the earlier of (A) the date that is three (3) months following the date of such cessation of Employment, or (B) the Final Exercise Date, and except to the extent previously exercised as permitted by this Section 3(c)(i) will thereupon immediately terminate.

(ii) Subject to clause (iii) below and Section 4 of this Agreement, the SAR, to the extent vested prior to the cessation of the Grantee's Employment due to death, will remain exercisable until the earlier of (A) the first anniversary of the Grantee's death or (B) the Final Exercise Date, and except to the extent previously exercised as permitted by this Section 3(c)(ii) will thereupon immediately terminate.

(iii) If the Grantee's Employment is terminated by the Company and its subsidiaries in connection with an act or failure to act constituting Cause (as the Administrator, in its sole discretion, may determine), or such termination occurs in circumstances that in the determination of the Administrator would have entitled the Company and its subsidiaries to terminate the Grantee's Employment for Cause, this SAR (whether or not vested) will immediately terminate and be forfeited upon such termination.

Notwithstanding the foregoing, to the extent the Grantee is a party to an Executive Severance Agreement or other written agreement with the Company that provides for the SAR to remain outstanding and continue to vest during a specified period of time following the Grantee's cessation of Employment (such period, the "Severance Period"), the SAR shall remain outstanding and shall continue to vest in accordance with the terms of this Agreement during the Severance Period as if the Grantee had remained employed during such period, subject to any conditions on continued vesting as may be contained in such Executive Severance Agreement or other written agreement. Any portion of this SAR that vests during such Severance Period will remain exercisable until the earlier of (A) the date that is three (3) months following the date that is the last day of such Severance Period, or (B) the Final Exercise Date, and except to the extent previously exercised as permitted by this Section 3(c) will thereupon immediately terminate. For the avoidance of doubt, any portion of the SAR that fails to vest during the Severance Period will immediately be forfeited on the last day of such period.

(d) Extension of Exercise Period. Notwithstanding anything in Section 3(b) or 3(c) to the contrary, if, as of the Final Exercise Date or the last date during the period specified in Section 3(c)(i), as applicable, the Grantee is prohibited by applicable law or written Company policy applicable to similarly situated employees from engaging in any open-market sales of Stock, the Final Exercise Date or such period specified in Section 3(c)(i), as applicable, will be automatically extended to that date that is thirty (30) days following the date the Grantee is no longer prohibited from engaging in such open-market sales.

4. Forfeiture; Recovery of Compensation.

(a) The Administrator may cancel, rescind, withhold or otherwise limit or restrict the SAR at any time if the Grantee is not in compliance with all applicable provisions of this Agreement and the Plan, or if the Grantee breaches any agreement with the Company or its subsidiaries with respect to non-competition, non-solicitation, invention assignment or confidentiality, including, but not limited to, any employment agreement or offer letter with the Company or the Company's standard Employee Agreement (Confidentiality, Non-Solicitation, Non-Competition and Developments Agreement).

(b) By accepting the SAR, the Grantee expressly acknowledges and agrees that his or her rights, and those of any permitted transferee of the SAR, under the SAR, including to any Stock acquired under the SAR or proceeds from the disposition thereof, are subject to Section 6(a)(5) of the Plan (including any successor provision). Nothing in the preceding sentence shall be construed as limiting the general application of Section 8 of this Agreement.

5. Transfer of SAR. The SAR may not be transferred except as expressly permitted under Section 6(a)(3) of the Plan.

6. Withholding. The exercise of the SAR will give rise to "wages" subject to withholding. The Grantee expressly acknowledges and agrees that the Grantee's rights hereunder, including the right to be issued Shares upon exercise, are subject to the Grantee promptly paying to the Company in cash (or by such other means as may be acceptable to the Administrator in its discretion) all taxes required to be withheld. No Shares will be transferred pursuant to the exercise of this SAR unless and until the person exercising this SAR has remitted to the Company an amount sufficient to satisfy any federal, state, or local withholding tax requirements, or has made other arrangements satisfactory to the Company with respect to such taxes. The Grantee authorizes the Company and its subsidiaries to withhold such amount from any amounts otherwise owed to the Grantee, but nothing in this sentence shall be construed as relieving the Grantee of any liability for satisfying his or her obligation under the preceding provisions of this Section.

7. Effect on Employment. Neither the grant of the SAR, nor the issuance of Shares upon exercise of the SAR, will give the Grantee any right to be retained in the employ or service of the Company or any of its Affiliates, affect the right of the Company or any of its Affiliates to discharge or discipline such Grantee at any time, or affect any right of such Grantee to terminate his or her Employment at any time.

8. Provisions of the Plan. This Agreement is subject in its entirety to the provisions of the Plan, which are incorporated herein by reference. A copy of the Plan as in effect on the Date of Grant has been furnished to the Grantee. By exercising all or any part of the SAR, the Grantee agrees to be bound by the terms of the Plan and this Agreement. In the event of any conflict between the terms of this Agreement and the Plan, the terms of the Plan shall control.

9. Provisions of Executive Severance Agreement. To the extent the Grantee has entered into an Executive Severance Agreement with the Company, for so long as such Executive Severance Agreement remains in effect, the terms of such Executive Severance Agreement as they relate to the SAR shall control in the event of any conflict with the terms of this Agreement.

10. Acknowledgements. The Grantee acknowledges and agrees that (i) this Agreement may be executed in two or more counterparts, each of which shall be an original and all of which together shall constitute one and the same instrument, (ii) this agreement may be executed and exchanged using facsimile, portable document format (PDF) or electronic signature, which, in each case, shall constitute an original signature for all purposes hereunder and (iii) such signature by the Company will be binding against the Company and will create a legally binding agreement when this Agreement is countersigned by the Grantee.

[Signature page follows.]

IN WITNESS WHEREOF, the Company has caused this Agreement to be executed by its duly authorized officer.

AKEBIA THERAPEUTICS, INC.

By:_____

Name: [•]
Title: [•]

Dated:

Acknowledged and Agreed:

By:
[Grantee's Name]_____

Schedule A
Time Vesting Schedule

The SAR, unless earlier terminated or forfeited, will vest, subject to Grantee's continuous Employment though the applicable vesting date, (i) as to 25% of the total number of Shares subject to the SAR on the first anniversary of the Date of Grant; and (ii) as to the remaining 75% of Shares subject to the SAR, ratably on the first day of each calendar quarter between the one-year anniversary of the date of grant and the fourth anniversary of the Date of Grant.

Exhibit 31.1

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, John P. Butler, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Akebia Therapeutics, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: May 8, 2023

By: /s/ John P. Butler

John P. Butler
President, Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David A. Spellman, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Akebia Therapeutics, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: May 8, 2023

By: /s/ David A. Spellman

David A. Spellman

Senior Vice President, Chief Financial Officer and Treasurer

(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002 (18 U.S.C. Section 1350)

In connection with the accompanying Quarterly Report of Akebia Therapeutics, Inc. (the "Company") on Form 10-Q for the quarter ended March 31, 2023 (the "Report"), I, John P. Butler, as Chief Executive Officer and President of the Company, and I, David A. Spellman, as Senior Vice President, Chief Financial Officer and Treasurer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: May 8, 2023

By: /s/ John P. Butler
John P. Butler
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: May 8, 2023

By: /s/ David A. Spellman
David A. Spellman
Senior Vice President, Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)