

Risk Factors Comparison 2025-03-13 to 2024-03-14 Form: 10-K

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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, reputation, results of operations, financial condition and stock price which can be materially and adversely affected. 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 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 ~~may require~~ **requires** upfront capital expenditures and significant **research and development, or R & D**, expenses. Despite the investment in assets and R & D, 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, or R & D~~, including our preclinical and clinical development activities, commercializing Auryxia **and Vafseo** and providing general and administrative support for these operations. We have funded our operations principally through product sales, payments received from our collaboration and licensing partners, borrowings under term loans, sales of our common stock, including through our employee stock purchase plan, a working capital payment from Vifor (International) Ltd. (now a part of CSL Limited), or CSL Vifor, and a royalty transaction. Prior to our 2018 merger, or the Merger, with Keryx Biopharmaceuticals, Inc., or Keryx, whereby 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~~ **While we currently have two commercial products, we** are not currently profitable and we have incurred net losses each year since our inception, including a net loss of \$ ~~51.69~~ **9.4** million for the year ended December 31, ~~2023~~ **2024**. As of December 31, ~~2023~~ **2024**, we had an accumulated deficit of \$ ~~1.67~~ billion. We cannot guarantee when, if ever, we will become profitable. In March 2022, we received a complete response letter, or CRL, from the United States, or U. S., Food and Drug Administration, or FDA, regarding our new drug application, or NDA, for vadadustat, ~~our lead investigational product candidate, for the treatment of anemia associated with~~ **chronic kidney disease, or CKD. Following** ~~The FDA concluded that the data in the NDA did 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~~ **in 2022 for** and focused on the favorable balance between the benefits and risks of vadadustat, **we filed a resubmission to our NDA in 2023. On March 27, 2024, the FDA approved our NDA for vadadustat under the trade name Vafseo for the treatment of anemia due to CKD in adult adults patients who have been receiving dialysis for at least three months. However, we expended significant additional resources to obtain the approval of Vafseo, the commercialization of Vafseo was delayed and Vafseo was approved for a narrower indication than we initially pursued, which had and could continue to have an adverse effect** 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 May 2023, the Office of New Drugs, or OND, denied our appeal but provided a path forward for us to resubmit the NDA for vadadustat for the treatment of anemia due to CKD for dialysis dependent patients without the need for us to generate additional clinical data. In September 2023, we filed our resubmission to our NDA, and in October 2023, the FDA acknowledged that the resubmission was complete and set a user fee goal date, or PDUFA date, of March 27, 2024. There can be no assurances that we will 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. If we do not obtain approval of vadadustat in the U. S., or if the approval is delayed, it would have a material adverse impact on our business. Even 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 our ability to manage expenses and the overall success of Auryxia, **Vafseo 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: • ~~our ability to obtain approval for vadadustat in the U. S. in a timely manner or at all;~~ • obtaining adequate or favorable pricing and reimbursement from private and governmental payors for Auryxia, **Vafseo 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, **Vafseo 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 **Vafseo** 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; • ~~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, **Vafseo vadadustat, if approved**, and any other product, including those that may be in- licensed or acquired; • **obtaining regulatory approval for any label expansion for Vafseo, including the timing and scope thereof; • our ability to maintain contracts with dialysis organizations for the sale of Auryxia and Vafseo in the U. S.; • 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; Akebia Therapeutics, Inc. | Form 10- K | Page 50-49 • actual the timing and scope of marketing approvals or for any perceived advantages or disadvantages of our products or product candidates- candidate, if approved 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 those that may be therapies, based, in - licensed part, on their perception of our- or acquired 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, Vafseo vadadustat, if approved, and any other product and product candidate, including those that may be in- licensed or acquired; • the potential impact of geopolitical pressures or the BIOSECURE Act on our ability to conduct our business as currently conducted; • 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 collaborators' and our sales, marketing, manufacturing and distribution strategies and operations; • competing effectively with any products for the same or similar indications as our products (including generics); • maintaining, protecting and expanding our portfolio of intellectual property rights, including patents and trade secrets; and • the adverse impact of the recent COVID-19 pandemic on CKD patients and the phosphate binder market in which we compete. Our collaboration, license and other revenue also depends on our partners' ability to successfully market and sell vadadustat Vafseo and Auryxia in the territories in which they have licensed our products. For example, in May 2023, we entered into a license agreement with MEDICE Arzneimittel Pütter GmbH & Co. KG, or Medice, pursuant to which we granted Medice an exclusive license to develop market and commercialize vadadustat sell Vafseo for the treatment of anemia in patients with CKD chronic kidney disease in the European Economic Area, or the EEA, the United Kingdom, or UK, Switzerland and Australia, or Medice Territory. Vafseo is currently marketed and sold by Medice in certain countries in the Medice Territory. If Medice's launch of vadadustat Vafseo in certain countries in the Medice Territory is delayed or their sales are lower than anticipated, we may not receive the revenue that we expect from Medice on the timing anticipated, or at all. In addition July 2024, under we entered into a Termination and Settlement Agreement with CSL Vifor, or the Vifor Termination Agreement. Pursuant to the Vifor Termination Agreement, we agreed, among other things, to terminate, effective immediately, the Second Amended and Restated License Agreement that we entered into with CSL Vifor -in February 2022, as amended in May 2024, or the Vifor License Agreement, pursuant to which we granted CSL Vifor an exclusive license to sell vadadustat Vafseo 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 certain group purchase purchasing organizations, or GPOs, and to certain non- retail specialty pharmacies in the U. S., which represents a significant portion of the potential market for vadadustat Vafseo. If vadadustat As a result, we have regained our rights to sell Vafseo to Fresenius Kidney Care North America and is its approved, but CSL affiliates and certain other third- party dialysis organizations in the U. S. Pursuant to the Vifor License is not successful in commercializing vadadustat in a timely manner, or at all, our expected revenue related to vadadustat would be adversely impacted. In addition, pursuant to the Vifor Agreement, CSL Vifor contributed \$ 40. 0 million to a working capital facility, or Working Capital Fund, established to partially fund our costs of purchasing Vafseo pre-launch vadadustat inventory from our contract manufacturers. The amount available under Pursuant to the terms of the Vifor Termination Agreement, we have agreed to repay the Working Capital Fund to CSL Vifor through quarterly tiered royalty payments ranging from 8 % to 14 % of our net sales of Vafseo in the U. S., or the WCF Royalty Payments. The WCF Royalty Payments will commence on July 1, 2025, and will continue until the earlier of (i) the cumulative total of the WCF Royalty Payments equals \$ 40. 0 million, or (ii) May 31, 2028. The WCF Royalty Payments are subject to minimum true- up milestones of \$ 10. 0 million, \$ 20. 0 million and \$ 40. 0 million, or the WCF Royalty True- Up Payments, on each of May 31, 2026, May 31, 2027 and May 31, 2028, respectively, or the WCF Royalty True- Up Dates. If the cumulative total of the WCF Royalty Payments paid to CSL Vifor on any given WCF Royalty True- Up Date is reviewed at specified intervals and is adjusted based less than the respective WCF Royalty True- Up Payment, we will pay CSL Vifor a on-one - time payment equal to a number of factors including outstanding supply commitments for vadadustat for the U. S. difference between the WCF Royalty True- Up Payment and agreed upon vadadustat inventory levels held the cumulative total of the WCF Royalty Payments paid by us for the U through such WCF Royalty True- Up Date. S. Additionally If we are not successful in commercializing Vafseo, upon termination or expiration of the Vifor Agreement for any reason other than convenience by CSL Vifor (including following receipt of the CRL maintaining contracts with dialysis organizations on favorable terms, for- or vadadustat) at all, we will our expected revenue related to Vafseo would be adversely impacted and required to refund the outstanding balance of the Working Capital Fund on the date of termination or expiration. If we are required may be unable to repay all or part of the WCF Royalty Payments Working Capital Fund sooner than anticipated, it which could have a material adverse impact on our consolidated financial statements. Our ability to achieve profitability also depends on our ability to manage our expenses. We expect to continue to incur substantial additional operating expenses, including additional R & D expenses related to our pipeline, additional costs related to vadadustat, and R & D and selling, general and administrative expenses for ongoing development and commercialization of Auryxia and Vafseo, which could lead to operating losses for the foreseeable future. We will continue to incur substantial expenditures relating to continued commercialization and post- marketing requirements for Auryxia and

vadadustat, **Vafseo** if we are able to obtain marketing approval for vadadustat, and any other products, including those that may be in-licensed or acquired, as well as costs relating to the R & D of any other product candidate, including those that may be in-licensed or acquired. Our prior losses have had, and expected future losses will continue to have, an adverse effect on our stockholders' (deficit) equity and working capital. In addition to any further costs not currently contemplated in our operating plan, our ability to achieve profitability and our financial position will depend, in part, on the rate of our future expenditures, our ability to obtain approval for vadadustat in Akebia Therapeutics, Inc. | Form 10- K | Page 50 51 the U. S., the timing of our product revenue, collaboration, license and other revenue, the timing and amount of any repayment of the Working Capital Fund from CSL Vifor, our continued compliance with the terms of the BlackRock Credit Agreement and our ability to obtain additional funding, should it be needed. 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 our resubmission to our NDA, and any other product or product candidate, including those that may be in- licensed or acquired ; • conduct and enroll patients in any clinical trials, **as well as costs relating to** including post- marketing studies or any other **the R & D of Vafseo** 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. **Our prior losses have had, and expected future losses will continue to have, and an adverse effect on our stockholders' (deficit) equity vadadustat, if we are able to obtain marketing approval for vadadustat, and working capital. In addition to any further costs not currently contemplated in our operating plan, our ability to achieve profitability and our financial position will depend, in part, on the rate of our future expenditures, the timing of our product, collaboration, license and other product revenue**, including those **the timing** that may be in- licensed or acquired; • manufacture Auryxia, vadadustat and **amount of** 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; • repay, and pay any associated pre- payment **repayment of** penalties, if applicable, **the WCF Royalty Payments, our continued compliance with the term terms** loans in an aggregate principal amount of up to \$ 55. 0 million, or the Term Loans, as of January 29, 2024, that were made available to us pursuant to an Agreement for the Provision of a Loan Facility **, as amended**, or the BlackRock Credit Agreement, with Kreos Capital VII (UK) Limited, which are funds and accounts managed by BlackRock Inc., collectively, BlackRock **, and our ability to obtain additional funding, should it be needed. In addition, we expect to continue to incur significant expenses if and as we: • continue our commercialization activities for Auryxia, Vafseo and any other product or product candidate for which we obtain approval, including those that may be in- licensed or acquired; • seek regulatory approval for any label expansion for Vafseo; • conduct and enroll patients in any clinical trials, including post- marketing studies or any other clinical trials for Auryxia, Vafseo or any other product or product candidate, including those that may be in- licensed or acquired; • seek marketing approval for any product candidate, including those that may be in- licensed or acquired; • maintain marketing approvals for Auryxia, Vafseo and any other product, including those that may be in- licensed or acquired; • manufacture Auryxia, Vafseo 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; • repay, and pay any associated pre- payment penalties, if applicable, the term loans in an aggregate principal amount of up to \$ 55. 0 million, or the Term Loans, that were made available to us pursuant to the BlackRock Credit Agreement; • make royalty, milestone or other payments under our current and any future in- licensing 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 **expended** and **will continue to may in the future** expend significant resources on our legal proceedings, as described below under Part I, Item 3. Legal Proceedings, **or including** any other legal proceedings **that may be** brought by or against us in the future. 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 perform studies different from or larger than those currently planned, to conduct any additional clinical trials, whether in order to obtain approval or as a post- approval study, including **the post- approval studies required for Vafseo and any other** additional clinical trial that we decide to conduct for vadadustat **Vafseo**, **or** if there are any delays in completing **any of our clinical trials or if there these activities** are further delays in or issues with obtaining marketing approval for vadadustat in the U. S. beyond our PDUFA date. 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 or the associated revenue. 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, our product revenue, 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. In addition, our ability to generate revenue would be negatively affected if **dialysis organizations are unwilling to include Auryxia or Vafseo in their formulary or** 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, ~~we may generate product revenue from Vafseo in the U. S., generate royalties from Vafseo in Europe and other territories where it is approved, 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 may need to obtain additional financing to continue to fund our operating plan.~~ Akebia Therapeutics, Inc. | Form 10- K | Page 52-51 **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 may need to obtain additional financing to continue to fund our operating plan.** We may require substantial additional financing to fund our business. 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 December 31, ~~2023-2024~~, our cash and cash equivalents were \$ ~~42-51~~.9 million. We expect to continue to expend substantial amounts of cash for the foreseeable future as we continue to commercialize Auryxia; ~~pursue approval for vadadustat~~ **develop and commercialize Vafseo** in the U. S. ~~with the FDA and develop and commercialize vadadustat in the U. S., if approved~~; 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 R & D, 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 the outcome of our NDA resubmission~~, or to complete post- marketing studies for Auryxia and ~~Vafseo 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~~ **Vafseo** 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, ~~Vafseo 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, **label expansion**, 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~~ **Vafseo** or any other product candidates; • the outcome of our efforts to obtain marketing approval for ~~vadadustat in the U. S. 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, **label expansion for Vafseo or** marketing approvals for ~~vadadustat, including in the U. S. 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, **Vafseo** or any other product, including those that may be in- licensed or acquired; • the **timing and** number of generic versions of Auryxia that enter the market following loss of exclusivity, or LoE, for Auryxia ~~in on~~ March ~~20~~, 2025, **the pricing of generic versions of Auryxia** and the timing of, and the magnitude of, the impact on the product revenue from Auryxia, including 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~~ **Vafseo** 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 may need to obtain substantial additional financing to fund our business. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our R & D programs or any future commercialization efforts ~~. We failed to timely file our Quarterly Report on Form 10- Q for the three months ended June 30, 2023, or the Second Quarter 10- Q. Because of that failure to file, we are not currently eligible to file or use a Registration Statement on Form S-3. This may make it more difficult for us to conduct a public offering of our securities.~~ Akebia Therapeutics, Inc. | Form 10- K | Page ~~53-52~~ We believe our existing cash resources and the cash we expect to generate from product, royalty, supply and license revenues ~~as well as the borrowings and potential future borrowings that are available under the BlackRock Credit Agreement and the working capital liability~~ are sufficient to fund our current operating plan for at least twenty- four months ~~if vadadustat is approved in the U. S and for at least twelve months from filing the Form 10- K, if vadadustat is not approved in the U. S.~~ However, if our operating performance deteriorates significantly from the levels expected in our operating plan ~~, or if vadadustat is not approved in the U. S.~~, it would have an adverse effect on our liquidity and capital resources and could affect 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 the BlackRock Credit Agreement, and the loan is accelerated, or if certain pre- specified events occur and we are required to make

principal payments to BlackRock sooner than we currently anticipate, such event could have a material adverse effect on our business. 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 and cash we expect to generate 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, Vafseo and any other products or product candidates, including vadadustat and 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. In addition, raising funds in the current economic environment may present additional challenges. For example, any sustained disruption in the capital markets from adverse macroeconomic conditions and an uncertain geopolitical environment, such as rising inflation, increasing interest rates, slower economic growth or recession, global supply chain disruptions, the ongoing Russia-Ukraine war, the Israel-Hamas war and the war in the Middle East and tensions between China and Taiwan, could negatively impact our ability to raise capital, and we cannot predict the extent or duration of such macroeconomic disruptions. 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, Vafseo and any other products or product candidates, including vadadustat and 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 products and product candidates on unfavorable terms to us. We expect to finance future cash needs through product revenue and royalty and license revenue, and we may seek to sell public or private equity, enter into new debt transactions, explore potential strategic transactions or a combination of these approaches or other strategic alternatives. 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. For example, since September 12, 2024 (the date our shelf registration statement on Form S-3 went effective) through December 31, 2024, we sold 14,271,631 shares of our common stock in an at-the-market offering with gross proceeds of \$ 24.3 million. 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 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 to develop and commercialize Auryxia and Vafseo, 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 R & D programs may initially show promise, yet fail to yield product candidates for clinical development. Our commercialization for may many reasons, including the following: • the research methodology used may not be successful in identifying potential indications and / the price of our or product candidates; common stock and our ability to access..... on the OTC Markets or another quotation. Akebia Therapeutics, Inc. | Form 10-K | Page 53 54 medium; depending on our ability to meet the specific listing requirements of those quotation systems. As a result, an investor would likely find it more difficult to trade or obtain accurate price quotations for our shares. Delisting would likely also reduce the visibility, liquidity, and value of our common stock, reduce institutional investor interest in our Company, and may increase the volatility of our common stock. Delisting could also cause a loss of confidence of potential industry partners, lenders, and employees, which could further harm our business and our future prospects. On May 9, 2023, we received a letter from Nasdaq stating that we had not regained compliance with the minimum bid price rule during the compliance period and was subject to delisting. On May 22, 2023, we received a letter from the Office of General Counsel of Nasdaq informing us that Nasdaq confirmed that we had regained compliance with the \$ 1.00 per share minimum bid price requirement. On August 11, 2023, we received a notification letter from Nasdaq informing us that since we had not yet filed our Second Quarter 10-Q, we are not in compliance with Nasdaq's listing rule requiring timely filing of all required periodic financial reports with the U. S. Securities and Exchange Commission, or the SEC. On August 30, 2023, we received a letter from the Office of General Counsel of Nasdaq informing us that Nasdaq confirmed that we had regained compliance with Nasdaq's listing rule requiring timely filing of all required periodic financial reports with the SEC. Although the minimum bid price deficiency and Nasdaq periodic reporting requirement matters are now closed, there can be no assurance that we will be able to continue to comply with the Nasdaq continued listing requirements. 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 the pursuit of approval for vadadustat in the U. S. with the FDA, 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 R & D 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 R & D efforts for one or more of our programs, or we may not be able to identify, discover, develop or commercialize additional product candidates, including those that may be in- licensed or acquired, 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 have focused on products, research programs and product candidates for specific indications. As a result, we have had to, and in the future may need to, forgo or delay pursuit of opportunities with other product candidates or for other indications, or may 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 R & D 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 ~~Akebia Therapeutics, Inc. | Form 10- K | Page 55~~ technology to us. As a result, our rights to these product candidates may be limited or we may be required to make future payments to such third parties if we are successful in developing such product candidates. 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 **Akebia Therapeutics, Inc. | Form 10- K | Page 54** 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, **or** the Cycleron Agreement, with Cycleron Therapeutics Inc., or Cycleron, pursuant to which Cycleron granted us an exclusive global license under certain intellectual property rights to research, develop and commercialize praliguat, an investigational oral soluble guanylate cyclase, ~~or sGC, stimulator~~. **In December 2024, we entered into an amendment to the Cycleron Agreement, pursuant to which we amended the terms of the Cycleron Agreement, and we now control all clinical and commercial manufacturing of praliguat, which will be conducted by a third party manufacturer**. Although we have progressed preclinical studies for praliguat, we need to do additional work to manufacture product for clinical trials than originally anticipated before we can initiate the trials, and when the clinical trials are started, we may be unsuccessful in developing praliguat. If any of the assumptions that we made in valuing the transaction, including the costs or timing of development of praliguat as a result of the additional manufacturing work or otherwise, or the potential benefits of praliguat, 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; ~~Akebia Therapeutics, Inc. | Form 10-K | Page 56~~ • 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.

Risks Related to our Financial Arrangements Our obligations in connection with the BlackRock Credit Agreement and requirements and restrictions in the BlackRock Credit Agreement could adversely affect our financial condition and restrict our operations. We entered into the BlackRock Credit Agreement, which provides for a senior secured term loan facility, in the aggregate principal amount of up to \$ 55.0 million, or the Term Loan Facility. The initial tranche of \$ 37.0 million, or the Tranche A Loan, closed on January 29, 2024, or the Closing Date. ~~In addition to the Tranche A Loan, an the Term Loan Facility includes additional amount of tranches available as follows: \$ 8.0 million available in a single draw through December 31, 2024, or the Tranche B Loan, was drawn on April 19, 2024, and an additional \$ 10.0 million was available in a single draw drawn through December 31 on February 3, 2024-2025, or the Tranche C Loan and, together with the Tranche A Loan and the Tranche B Loan, the Term Loans. See Note 7, Indebtedness, to our audited consolidated financial statements in Part II, Item 8. Financial Statements of this Form 10-K for additional information regarding our obligations under the BlackRock Credit Agreement. Each Term Loan draw is subject to various conditions precedent, including (x) the absence of any defaults or events of default and our continued compliance with the terms and provisions of the BlackRock Credit Agreement, (y) in the case of the Tranche B Loan and Tranche C Loan, receipt of marketing approval for vadadustat from the FDA, and (z) in the case of Tranche C, receipt of a certain amount of cumulative gross cash proceeds after the Closing Date in the form of equity or equity linked securities in one or more series of transactions. The Term Loan Facility has had an initial maturity date of March 31, 2025, which was will be automatically extended to January 29, 2028 if, or the Maturity Date, since we receive-received FDA approval on or for Vafseo prior to June 30, 2024, or the Maturity Date. If vadadustat is not approved by the FDA by June 30, 2024, we will be required to repay the Term Loan Facility sooner than anticipated.~~ The BlackRock Credit Agreement contains certain representations and warranties, affirmative covenants, negative covenants, financial covenants, events of default and other provisions and conditions that are customarily required for similar financings. The financial covenants under the BlackRock Credit Agreement require us to either (i) maintain cash and cash equivalents, measured as of the last day of each fiscal month, greater than or equal to \$ 15.0 million or (ii) earn consolidated revenue, measured as of the last day of each fiscal month for the trailing twelve-month period, of \$ 150.0 million. Failure to maintain compliance with these or other covenants would result in an event of default under the BlackRock Credit Agreement, which ~~Akebia Therapeutics, Inc. | Form 10-K | Page 55~~ could result in enforcement action, including acceleration of amounts due under the BlackRock Credit Agreement, or limit our ability to make certain payments under the Vifor Termination Agreement. The Term Loan Facility will accrue interest at a floating annual rate equal to the sum of (x) term Secured Overnight Financing Rate for a tenor of one month (subject to a floor of 4.25 % per annum) plus (y) a margin of 6.75 % per annum (subject to an overall cap of 15.00 % per annum on the all-in interest rate). During the continuance of any payment event of default under the BlackRock Credit Agreement, the interest rate on such overdue sum will automatically increase by an additional 3.0 % per annum, and may be subject to an additional late fee of 2.0 % of such overdue sum. The Term Loan Facility does not amortize during the period commencing on the Closing Date and ending on December 31, 2025 (which was extended to December 31, 2026 at our option), or the Interest Only Period. We are required to pay interest and, after the Interest Only Period, principal on the first calendar day of each month. In the event of certain prespecified events, the repayment schedule will be accelerated. ~~For example, if FDA approval is not obtained on or prior to June 30, 2024, the Interest Only Period will automatically terminate on October 1, 2024, and we will be required to repay the Term Loans in seven equal monthly payments (comprised of principal and interest), commencing on October 1, 2024 and ending on the Maturity Date. If any of these events occur, and we are required to repay principal sooner than we anticipate, it would have an adverse effect on our business. In the event there is an acceleration of our and certain of our subsidiaries' liabilities under the BlackRock Credit~~

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 BlackRock could seek to enforce security interests in the collateral securing the BlackRock Credit Agreement, which would have a material adverse effect on our business, financial condition and results of operations. **Akebia Therapeutics, Inc. | Form 10-K | Page 57** In addition, our obligations in connection with the BlackRock Credit 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, incurring certain additional indebtedness, creating certain liens, paying cash 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, R & D 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. In February 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 receive royalties and sales milestones for **vadadustat Vafseo**, 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 Vafseo** 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. 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 and **Vafseo vadadustat, if approved**. If we are unable to continue to successfully commercialize Auryxia **or vadadustat, if approved** and **commercialized Vafseo**, our results of 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 and **vadadustat Vafseo**. 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, **Vafseo and vadadustat, if approved**, and any other product or product candidate, including those that may be in- licensed or acquired. **If we are not able to maintain contracts with dialysis organizations and other customers for the sale of Auryxia and Vafseo on favorable terms, or at all, our revenue and results of operations will be adversely affected**. 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 **Akebia Therapeutics, Inc. | Form 10- K | Page 56** affected. **For example, the approval for Vafseo in the U. S. is limited to the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months instead of all such adults. This limitation could affect the level of market acceptance of Vafseo. We currently have exclusive rights under a series of patents and patent applications to commercialize Auryxia in the U. S. that protect us from generic drug competition until March 20, 2025. Following LoE, on March 20, 2025, the number of generic versions of Auryxia that enter the market, and the timing thereof, will adversely affect our revenue from Auryxia. The impact of LoE on future Auryxia revenues will depend on many factors, including our ability to maintain contracts with dialysis organizations, the timing and number of generics and the pricing of generics and other products on the market that compete with Auryxia. In addition, we believe the dynamics of Auryxia reimbursement being included in the ESRD bundle under Medicare Part B and Auryxia LoE could result in the buying pattern of certain customers in 2025 and future years being different than their historical practices. If Auryxia sales decline faster than we anticipate following LoE, our results of operations and financial condition will be materially harmed**. Given the concentration of dialysis clinics in large networks, with DaVita, Inc., or DaVita, and Fresenius Kidney Care Group LLC, **or Fresenius, and U. S. Renal Care, or USRC**, accounting for a vast majority of the dialysis population in the U. S., treatment is usually driven by medical protocols that are implemented across the entire network of clinics. Dialysis organizations require large data sets to adopt medical protocols. If dialysis organizations do not add **Vafseo vadadustat, if approved**, to their medical protocols in a timely manner, or at all, **our- or if the protocols service smaller populations than the current label, our results of** operations could be materially adversely affected. **If oral Oral - only** phosphate binders, including Auryxia, are included in the end- stage renal disease, or ESRD, Prospective Payment System, or PPS, bundle payment, **as of January 2025, however**, it will take time for dialysis organizations to implement internal mechanisms to dispense phosphate binders which could **negatively impact the market for phosphate binders, including Auryxia, and** divert **their-dialysis organizations'** attention from focusing on other therapeutic areas such as anemia management, which in turn could negatively impact the market for **Vafseo phosphate binders, including Auryxia**. In addition, dialysis organizations may choose lower cost binders over Auryxia, or binders that may have features or benefits more aligned with the dialysis organization's operational activities, which could negatively impact Auryxia revenue. **In addition, we currently have exclusive rights under a series of patents and patent applications to commercialize Auryxia in the U. S. that protect us from generic drug competition until March 2025. Following LoE in March 2025, the number of generic versions of Auryxia that enter the market will affect our revenue from Auryxia. We believe CMS' s 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. However, our ability to continue to generate revenue from sales of Auryxia following LoE will depend on many factors, including our ability to Akebia Therapeutics, Inc. | Form 10-K | Page 58 successfully contract with dialysis organizations, the timing and number of generics that enter the market and other products on the market that we compete with. If we are unable to maintain sales of Auryxia following LoE, our results of operations and financial condition will be materially harmed. We believe our revenue growth **has been** negatively impacted by the ~~recent~~ COVID- 19 pandemic ~~in~~ **since** 2021, 2022 and 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 also 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, 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 ~~recent~~ COVID- 19 pandemic on future revenues and revenue growth, the ~~recent~~ COVID- 19 pandemic and the ongoing impacts from the ~~recent~~ COVID- 19 pandemic continue to adversely and disproportionately impact CKD patients and the phosphate binder market. Therefore, we expect the impacts from the pandemic to continue to have a negative impact on our revenue growth for the foreseeable future. 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, **Vafseo** or any of our future products, ~~including vadadustat, if 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, **Vafseo vadadustat, if approved,** 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 to **dialysis organizations**, third party payors, pharmacy benefit managers, or PBMs, and governmental authorities ; **• the availability of discounts and rebates to dialysis organizations to facilitate access for patients; • use at dialysis organizations and their willingness to include or continue to include Auryxia or Vafseo in their formulary or protocols and the scope of such protocols**; • 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 partners are able to make regarding the safety and efficacy of the product; **Akebia Therapeutics, Inc. | Form 10- K | Page 57** • 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; • ~~for vadadustat, if approved,~~ **use at dialysis organizations and their willingness to include vadadustat in their protocols**; • 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 ; **• the success of, or withdrawal from the market of, competing products** ; • 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 partners' sales, marketing, manufacturing and distribution strategies and operations; and • the restrictions on the use of the product together with other medications, if any. In addition, our ability to generate net product revenue depends on our ability to control the expenses associated with commercializing a product, including internal expenses, manufacturing costs, rebates, product returns and other adjustments. We do not have control over many of the expenses required to commercialize our products, and if we experience increased costs or expenses, we may not be able to afford the commercial activities required to successfully commercialize our products, which could have an adverse effect on our business. In addition, our net product revenue requires judgement and includes estimates for rebates and product returns, which can fluctuate from quarter- to- quarter and year- over- year. If our net product revenue is lower than anticipated, including as a result of higher expenses **or product returns**, our business could be harmed. Several healthcare facilities, including DaVita, have previously restricted access for non- patients as a result of the ~~recent~~ COVID- 19 pandemic, resulting in restricted access for certain members of our sales force : ~~As a result, we continue to engage with some healthcare providers and other customers virtually where possible. The restrictions on our customer- facing Akebia Therapeutics, Inc. | Form 10- K | Page 59 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.~~ Such precautionary measures have since been relaxed at certain healthcare facilities and, as a result, members of our sales force have resumed in person interactions with those customers. Nevertheless, some restrictions remain ; and **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 Vafseo. In addition,** 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 , **or due to outbreak of other infectious diseases, such as H1N1 virus (Swine Flu) and H5N1 virus (bird flu)** . Given this uncertain environment and the disproportionate impact of the ~~recent~~ COVID- 19 pandemic on CKD patients, we are actively monitoring the demand in the U. S. for Auryxia and **Vafseo** ~~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. 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, **Vafseo vadadustat, if approved,** or any other product candidates that may be approved. In order to

market Auryxia, **Vafseo** 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 U. S. for Auryxia, ~~our only commercial product. However, following receipt of the CRL, we implemented a reduction of our workforce in April and Vafseo May 2022 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, and we shifted to a strategic account management focused model for our commercial efforts.~~ If the remaining sales and marketing team cannot successfully commercialize Auryxia, ~~or Vafseo~~ if additional sales and marketing employees decide to leave, it could have a material adverse effect on Auryxia ~~our product~~ 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., with incremental additional hires in our sales force and medical affairs department, but if we are unable to do so successfully it 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 ~~or market acceptance~~ 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 and marketing team to a greater extent or earlier than we currently plan and at a higher already have, which would increase our cost costs more~~ 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 for vadadustat in the timeframe we expect, or at all.~~ We devote significant effort 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. ~~If key sales~~ Further, ~~our reductions in workforce may further exacerbate these conditions and marketing employees decide~~ interfere with our ability to ~~leave~~ find and retain qualified personnel. As a result, we may not be able to ~~retain our existing employees or hire and train~~ 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; **Akebia Therapeutics, Inc. | Form 10- K | Page 58**
- 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, **Vafseo vadadustat, if approved,** and any other product candidate that may be approved. **Furthermore Also,** 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 **Vafseo vadadustat, if approved.** For example, if, in connection with the Vifor Agreement, we experience difficulties with CSL Vifor, or if CSL Vifor is not successful in commercializing vadadustat, if approved, in the dialysis organizations for which they are responsible in a timely manner, or at all, our revenue related to vadadustat will be adversely impacted. **Akebia Therapeutics, Inc. | Form 10- K | Page 60**

Our, or our partners', failure to obtain or maintain adequate coverage, pricing and reimbursement for Auryxia, **Vafseo 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 **Vafseo, 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, **dialysis organizations**, 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, **Vafseo 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 successfully commercialize certain of our products. Coverage and reimbursement by a governmental authority, **dialysis organization,** third- party payor or PBMs 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, **dialysis organization,** 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 U. S., 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 **Advantage and / or** Part D plans and / or PBMs operating on behalf of **such 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 was~~ covered by Medicare under Part D **until January 1, 2025**, for the treatment of patients with hyperphosphatemia. In January 2011, CMS implemented the ESRD PPS, a prospective payment system for dialysis treatment. Under the ESRD PPS, CMS generally makes a single bundled payment to the dialysis facility for each dialysis treatment that covers all items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare- certified ESRD facilities or at their home. ~~As The inclusion of oral medications without injectable or intravenous equivalents such as Auryxia in the bundled payment was initially delayed by CMS until January 1, 2014, and through several subsequent legislative actions has been delayed until January 1, 2025. Absent further legislation or regulation on this matter, beginning in January 2025, oral ESRD- related drugs without injectable or intravenous equivalents, including Auryxia and all other phosphate lowering medications, are will be included in the ESRD bundle and separate Medicare payment for these drugs will are no longer be available . In addition, as dialysis organizations will receive a Transitional Drug Add- on Payment Adjustment, or TDAPA, payment for claims that include phosphate binders for the next two years. Vafseo, which we began selling in January 2025, is also included in the ESRD bundle and ease today under Medicare Part D- ESRD facilities will may nonetheless receive a TDAPA for Vafseo as a new renal dialysis drugs- drug meeting and biological products that meet certain criteria for a period of at least two years starting on January 1, 2025 . The TDAPA will provide provides separate payment based on the drug ' s Average Sales Price, or ASP, that will be in addition to the base rate in order to facilitate the adoption of innovative therapies. If There can be no assurances that CMS will not again delay the inclusion of these -- the oral ESRD- related drugs in the bundled payment. Even TDAPA reimbursement amount for Auryxia or Vafseo is lower than anticipated, or if Auryxia the TDAPA is eliminated deemed eligible by CMS-, revenue for sales of Auryxia could be significantly less in the TDAPA period than it would have an adverse impact on our revenue be if Auryxia is not bundled into the ESRD PPS. Moreover Additionally, in the post- TDAPA period, CMS currently expects to increase the single bundled payment base rate paid to the dialysis facility for each dialysis treatment to reflect that bundled oral only phosphate lowering drugs will be reimbursed as part of the single bundled payment for Medicare patients. However, There there can be no assurances that any increase in the single bundled payment base rate will be sufficient to Akebia Therapeutics, Inc. | Form 10- K | Page 59 adequately reimburse the dialysis facilities for Auryxia or Vafseo at a price that allows us to continue to sell Auryxia or Vafseo at a profit. In July 2024, Ardelyx, Inc., or Ardelyx, filed a complaint in the United States District Court for the District of Columbia against the U. S. Department of Health and Human Services, or HHS, CMS and other parties, which alleged that CMS' s plan to include oral- only phosphate lowering therapies in the ESRD PPS violated its statutory and regulatory authority under the Medicare Improvements for Patients and Providers Act, which established the ESRD PPS bundled payment system for dialysis services. In October 2024, Ardelyx filed a motion for a preliminary injunction to enjoin CMS from including oral- only phosphate lowering therapies in the ESRD PPS. CMS had earlier filed a motion to dismiss the complaint on jurisdictional grounds. On November 8, 2024, the district court denied Ardelyx' s motion for a preliminary injunction and it granted the government' s motion to dismiss. Thereafter, Ardelyx moved for reconsideration, but the district court also denied that request. On December 26, 2024, Ardelyx filed a notice of appeal with the US Court of Appeals for the DC Circuit. If Ardelyx is profitable successful in its claims, oral- only phosphate lowering therapies, including Auryxia, may be removed from the ESRD bundle, which could reduce anticipated revenue for us Auryxia . In addition, 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 not on dialysis, or 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 anemia due to CKD in patients on dialysis, or 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. We decided beginning in 2022 to terminate certain Part D contracts, as patients no longer had the access benefit given the prior authorization , or PA, requirement. Now patients must go through a medical exemption process, which is very similar to a prior authorization review. While we believe this had, and may continue to have, a negative Akebia Therapeutics, Inc. | Form 10- K | Page 61 impact on our overall sales volume, we believe it had a significant positive impact on our net selling price. However, if we experience additional negative impacts on our sales volume as a result of this change, it could have a negative impact on our product revenue. 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 will be required to enter into contracts with dialysis organizations, GPOs, 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 dialysis organizations, GPOs, 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, dialysis organizations, GPOs, third party payors, PBMs and / or 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 Three distributors, Fresenius Medical Care Rx, McKesson Corporation , Cardinal Health, Inc. and Cencora, Inc., formerly known as AmerisourceBergen Drug Corporation, in the aggregate, accounted for a significant percentage of our gross revenue during the year ended December 31, 2023-2024 . However, due to a variety of factors, including coverage of our products in the ESRD bundle and to support commercial availability of Vafseo in 2025, there were changes to the manner in which we distributed our products, which we implemented in January 2025. This included, for example, reducing the number of mainline wholesalers in our distribution network, distribution of products through specialty distributors, and an increased focus on direct sales through contracts with dialysis organizations . If we are not able to enter into and maintain agreements our arrangements~~

with these key **wholesalers, specialty distributors, the dialysis organizations and other purchasers for the sale of our products** on favorable terms, on a timely basis or at all, or if **dialysis organizations or there- other** is any adverse change in one **purchasers do not purchase as much product as we anticipate or terminate** or **our arrangements** more of these distributors' business practices or financial condition, it would adversely impact the market opportunity for **Auryxia-our products**, our product revenues and operating results. In addition, 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. Furthermore, vadadustat was approved in Europe and Australia for the treatment of anemia due to CKD in DD-CKD patients. In Europe, reimbursement is obtained on a country-by-country basis and it is a time-consuming process. Medice is working on securing pricing and reimbursement in key markets in Europe, but there is no guarantee of the timing or extent of reimbursement that they **the** will receive, if at all. 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, but reimbursement under TDAPA it is subject to review and approval by CMS. For those that obtain dialysis through commercial insurance during the 30-month coordination period or through Medicaid prior to Medicare becoming primary payor 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 six months following filing acceptance, 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 U. S., we expect it to be included in the fixed reimbursement model for a bundle of dialysis services, or the bundle, which will require us 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-three** providers: DaVita and **Fresenius Medical Care and USRC**, which account for a vast majority of the dialysis population in the U. S. Under the Vifor 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 U. S. We refer to Fresenius Medical Care North America and its affiliates, these organizations and specialty pharmacies collectively as the "Supply Group." See Note 8, Deferred Revenue, Refund Liability and Liability Related to Sale of Future Royalties, to our consolidated financial statements in Part II, Item 8. Financial Statements of this Form 10-K for additional information regarding the Vifor Agreement. If vadadustat is approved, and we are not able to maintain the Vifor Agreement or enter into a supply agreement **agreements** with DaVita or **these, and other**, dialysis **organizations elinies, or for the** if Vifor is not able **sale** to successfully contract with the Supply Group **of Vafseo on favorable terms, in a timely matter or at all**, 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 **Akebia Therapeutics, Inc. | Form 10-K | Page 62** contract with a drug manufacturer for a specific product **, or will terminate their contract**, resulting in that product not being on that organization's formulary. If any dialysis organization does not add **Auryxia or Vafseo** vadadustat, if approved, to **the formulary, or removes Auryxia or Vafseo from** the formulary, our business may be materially harmed. **Akebia Therapeutics, Inc. | Form 10- K | Page 60** In addition, we may be unable to sell Auryxia or **Vafseo** 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 **, including Medicare Advantage plans**, are central to patient and provider acceptance of any products for which we receive marketing approval. Existing competitive products may enter into sole source agreements with dialysis providers that impact the ability for new product innovations and new competitors may face price pressure based on existing contracts with dialysis providers. Further, in many countries outside the U. S., 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 U. S. 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. In addition, we plan to rely on a partner to obtain approval by reimbursement authorities outside the U. S. Our partners 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 partners' control. **Vafseo 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. Furthermore, Vafseo was approved in Europe and Australia for the treatment of anemia due to CKD in DD-CKD patients. In Europe, reimbursement is obtained on a country-by-country basis and it is a time consuming process. In May 2023, we entered into the license agreement with Medice, pursuant to which we granted Medice an exclusive license to develop and commercialize vadadustat **Vafseo** for the treatment of anemia in patients with **CKD chronic kidney disease** in the Medice Territory. **Medice launched and has received pricing and reimbursement for Vafseo in certain countries in Europe and is working on launching and securing pricing and reimbursement for Vafseo in other markets across Europe. There is no guarantee of the timing or extent of reimbursement that they will receive in each country, if at all.** If Medice is not able to obtain favorable pricing in the Medice Territory, or if such approvals are delayed, it will affect Medice's sales of vadadustat **Vafseo** in the Medice Territory, 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, **Vafseo vadadustat, if approved,** and any other product or product candidate, including those that may be in-licensed or acquired. Our objective is to **successfully continue to commercialize Auryxia and Vafseo** 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. If existing or new competitors of Auryxia **or Vafseo** take market share from us, it could have an adverse impact on **our revenue and our business. We currently have exclusive rights under a series of patents and patent applications to commercialize Auryxia in the U. S. that protect us from generic drug competition until March 20, 2025. Following LoE, in March 2025, the timing and number of generic versions of Auryxia that enter the market will affect our revenue from Auryxia. We and our licensors, Panion & BF Biotech, Inc., our or business Panion, and, as applicable, Dr. Hsu, entered into settlement agreements with all 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 U. S. beginning on March 20, 2025 (subject to FDA approval). On February 5, 2025, we entered into an Authorized Generic Distribution and Supply Agreement with Mylan Pharmaceuticals, Inc., or AG Partner, pursuant to which, on or after March 20, 2025, they will sell an authorized generic version of Auryxia. The impact of LoE on future Auryxia revenues will depend on many factors, including our ability to maintain contracts with dialysis organizations, the timing and number of generics and the pricing of generics and other products on the market that compete with Auryxia. In addition, we believe the dynamics of Auryxia reimbursement being included in the ESRD bundle under Medicare Part B and Auryxia LoE could result in the buying pattern of certain customers in future years being different than their historical practices. If Auryxia sales decline faster than we anticipate following LoE, our results of operations and financial condition will be materially harmed.** Auryxia is competing in the hyperphosphatemia market in the U. S. 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 **Akebia Therapeutics, Inc. | Form 10-K | Page 61** are in development, including OPKO Health Inc.'s Alpharen™ Tablets (fermagate tablets) and Unicycive's RENAZORB™ (lanthanum dioxycarbonate), or could otherwise enter the market that may impact the market for Auryxia. In October 2023, the FDA approved XPHOZAH® (tenapanor), a phosphate absorption inhibitor that is marketed by Ardelyx, Inc., and indicated to reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy, which may **adversely** impact the market for Auryxia. Auryxia is competing in the IDA market in the U. S. with over-the-counter oral iron, ferrous sulfate, other prescription oral iron formulations, including ferrous gluconate, ferrous fumarate, 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 Feracru® (ferric maltol), which is available in Europe for the treatment of IDA and Accrufer® (ferric maltol), which was launched in the U. S. for the treatment of IDA in July 2021. **In Japan, our Japanese sublicensee, Japan Tobacco International, or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize Riona (ferric citrate hydrate). In the hyperphosphatemia market, Riona competes with Fosrenol® (lanthanum carbonate hydrate) marketed by Bayer Yakuhin Ltd., generic lanthanum carbonate hydrate products, and Phozevel® (tenapor hydrochloride) marketed by Kyowa Kirin Co., Ltd. In the IDA market in Japan, Riona competes with Ferromia® (sodium ferrous citrate) marketed by Alfresa Pharma Corporation and Fero-Gradumet® (dried ferrous sulfate) marketed by Viatris Inc.** 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 our 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~~

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 Vafseo, which has been approved and is being marketed by MTPC in Japan under the trade name Vafseo. **In May 2023, we entered into the license agreement with Medice, pursuant to which we granted Medice an exclusive license to develop and commercialize Vafseo for the treatment of anemia in patients with CKD in the Medice Territory. Pursuant to the license agreement, we transferred the marketing authorization issued by the EMA, UK, the Swiss Agency for Therapeutic Products and the Australian Therapeutic Goods Administration to Medice.** We also granted Averoa SAS, or Averoa, an exclusive license to develop and commercialize ferric citrate in the EEA, Turkey, Switzerland, and the UK. **In 2023, Balkans** the marketing authorization for vadadustat was granted by the EMA, the United Kingdom Medicines and Healthcare Products Regulatory Agency, or the MHRA, the Swiss Agency for Therapeutic Products, or Swissmedic, and the Australian Therapeutic Goods Administration, or TGA. **In May 2023, we entered into the license agreement with Medice, pursuant to which we granted Medice an and exclusive license to develop certain countries in Eastern Europe and commercialize vadadustat the Middle East, for or the Averoa** treatment of anemia in patients with chronic kidney disease in the Medice Territory, and we transferred the marketing authorization issued by the EMA and Swissmedic to Medice. We will transfer the other marketing authorizations for the Medice Territory to Medice, if approved. In addition, we have conducted and in the future **may plan to** conduct clinical trials outside of the U. S. 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 Vafseo outside the U. S., 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 U. S.; • 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, increasing interest rates, 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; and • business interruptions resulting from geopolitical actions, including war and terrorism, global pandemics, or natural disasters including earthquakes, typhoons, floods and fires. **Akebia Therapeutics, Inc. | Form 10-K | Page 63** 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 Euro, the Pound Sterling and the Swiss Franc**. The exchange rates between **the these currencies** 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 these currencies** Japanese yen depreciates **depreciate** 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. **Akebia Therapeutics, Inc. | Form 10-K | Page 65** 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 of vadadustat and any other **of our** 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 Vafseo and **other our** product candidates or to successfully obtain approval of vadadustat **label expansion or for other Vafseo or approval of our** 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 **product** 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 **the INNO2VATE and vadadustat program; however, while Vafseo** achieved the primary and key secondary efficacy **endpoint endpoints** in each of the two PRO2TECT studies, **but** the PRO2TECT 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 For example**, in March 2022, we received the CRL for vadadustat Vafseo indicating that the FDA had determined that it could not approve the NDA in its present form, thus delaying any potential approval of vadadustat Vafseo. **In October Following submission of the FD RR to the FDA in 2022, we filed submitted the FD RR to the FDA. In May 2023, the OND denied our appeal but provided a resubmission path forward for us to our resubmit the NDA for vadadustat for the treatment of anemia due to CKD for dialysis dependent only in adult DD-CKD patients in** without the need for us to generate additional clinical data. **In September 2023,**

On [redacted], we filed our resubmission to our NDA, and in October 2023, the FDA acknowledged that the resubmission was complete and set a PDUFA date of March 27, 2024, the FDA approved our NDA for vadadustat under the trade name of Vafseo for the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months. However, it we expended significant additional resources to obtain the approval of Vafseo, the approved indication is impossible limited to predict when the treatment of anemia due to CKD in adults who have been receiving dialysis or for at least 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. If we are unsuccessful in obtaining approval for vadadustat in the three U. S. months and the commercialization of Vafseo was delayed, it which had and would could continue to have an adverse effect on our business results of operations. We Beyond seeking U. S. approval, we have several lifecycle management and indication label expansion opportunities currently under evaluation for vadadustat Vafseo, including one of which is the potential for alternative dosing, and another of which is label expansion for the treatment of anemia due to CKD in adult patients not on dialysis with NDD- CKD. However, we may will be required to complete additional clinical trials before seeking approval for label expansion for these the indications, which treatment of adult patients with NDD- CKD and we may be required to generate additional clinical data before seeking approval for alternative dosing. Clinical trials are time consuming and expensive, and even if vadadustat though Vafseo is approved as a treatment for adult patients with anemia due to CKD for on dialysis dependent patients for at least three months, we may not be successfully successful in any of these areas our lifecycle management or label expansion opportunities in the timeframe anticipated by us, or at all. For example, we plan to start a Phase 3 trial in the second half of 2025 to potentially expand Vafseo label to include the treatment of late-stage NDD- CKD patients; however, the FDA may not agree with our study design or we may not successfully demonstrate safety and / or efficacy needed to obtain regulatory approval or we may be unable to successfully complete the trial when anticipated, or at all. If the clinical trials for our label expansion opportunities are not successful or take longer than anticipated, or if we do not obtain FDA approval of label expansion for Vafseo for the treatment of adult patients with NDD- CKD or for alternative dosing in a timely manner, or at all, it could impact future revenue and have an adverse effect on our business. In addition, it is impossible to predict when or if any of our other product candidates will prove effective or safe in humans or will receive marketing approval or on what terms. 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 Vafseo 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..... or adverse side effects, failure to Akebia Therapeutics, Inc. | Form 10- K | Page 66-64 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 contract research organizations, or 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 or failure fail 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 expand or otherwise 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; **Akebia Therapeutics, Inc. | Form 10- K | Page 65** • we may be delayed in obtaining marketing approval for ~~vadadustat or our other~~ product candidates; • we may not obtain marketing approval for ~~vadadustat or our 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 Vafseo for~~ **potential future indications or any product candidate that is approved, 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, Vafseo 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 the success of our clinical trials. 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 began enrolling sites in a post- approval pediatric study for the Hyperphosphatemia Indication of Auryxia in the second quarter of 2022, which began patient recruitment in the third quarter of 2022, but enrollment of eligible pediatric patients in study sites continues to be very slow despite efforts to do so. 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. **Akebia Therapeutics, Inc. | Form 10- K | Page 66** 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, or FDORA, Congress required sponsors to develop and submit a diversity action plan, or DAP, 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. Specifically, action plans must include the sponsor' s goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft**

guidance from its website. As a result, the applicability of statutory obligations to submit DAPs and the agency's current thinking on best practices for clinical development remain unclear and we will need to carefully navigate such uncertainty. In addition, the regulatory landscape related to clinical trials in the European Union recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. We have conducted and intend to conduct certain of our clinical trials globally. However, there are additional risks unique to conducting trials outside of the U. S., and the FDA and other foreign equivalents may not accept data from such trials, in which case our development plans may be delayed, which could materially harm our business. We have conducted and intend to continue conducting certain of our clinical trials globally. The acceptance by the FDA or other regulatory authorities of data from clinical trials conducted outside their jurisdiction may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U. S. population and U. S. medical practice, (ii) the trials were performed by clinical investigators of recognized competence and pursuant to good clinical practice, or GCP, regulations and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, even where foreign clinical trial data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the clinical trial is well- designed and well- conducted in accordance with GCP requirements and the FDA is able to validate the data from the trial through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it could result in the need for additional trials, which could be costly and time- consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction. Conducting clinical trials outside the United States also exposes us to additional risks, including risks associated with: • additional foreign regulatory requirements; • foreign exchange fluctuations; • compliance with foreign manufacturing, customs, shipment and storage requirements; • cultural differences in medical practice and clinical research; Akebia Therapeutics, Inc. | Form 10- K | Page 67 licensed or acquired, or allow • diminished protection of intellectual property in some countries; and • interruptions, our – or delays 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 resulting from geopolitical, 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 war pediatric or elderly patients, due to a number of factors including parental or other caregiver considerations, concerns and burdens. For – or terrorism. example, we enrolled sites in a post- approval pediatric study for the Hypophosphatemia Indication of Auryxia in the second quarter of 2022. Vafseo which began patient recruitment in the third quarter of 2022, but enrollment of eligible pediatric patients in study sites continues to be very slow despite efforts to do so. 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 U. S., 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 U. S. 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 U. S. is subject to numerous additional risks unique to conducting business in jurisdictions outside the U. S., including: Akebia Therapeutics, Inc. | Form 10-K | Page 68 • 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 U. S. may not be accepted by the EMA, the PMDA and other regulatory authorities outside of the U. S. 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 U. S. 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 **Vafseo** 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 **Vafseo** in which the FDA concluded that the data in the NDA did not support a favorable benefit- risk assessment of vadadustat **Vafseo** 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, As a result, we submitted filed the FDRR and, following the FDRR, we filed a resubmission to our NDA, and the FDA and focused approved Vafseo on March 27, 2024. However, the approved indication is limited to favorable balance between the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult adults patients on who have been receiving 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 May 2023, the OND denied our appeal but provided a path forward for us to resubmit the NDA for vadadustat for the treatment of anemia due to CKD for dialysis dependent patients without the need for us to generate additional clinical data. In September 2023, we filed our resubmission to our NDA, and in October 2023, the FDA acknowledged that the resubmission was complete and set a PDUFA date of March 27, 2024. There can be no assurances that we will be successful in our NDA resubmission. If we are unable to overcome these concerns, vadadustat may not be approved by the FDA on favorable terms, or for at least three months all, and our financial condition could be materially harmed.** If we or others identify undesirable effects caused by, or other undesirable properties of, Auryxia, **Vafseo** 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 **or the boxed warning on Vafseo’s label regarding increased risk of death, myocardial infarction, stroke, venous thromboembolism and thrombosis of vascular access**; • 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; **Akebia Therapeutics, Inc. | Form 10-K | Page 69** • 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 Vafseo** 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 Vafseo** 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 the projected** patient populations for **vadadustat, if approved, that will be treated with Vafseo** 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 INNO2VATE Phase 3 program, the incidence of treatment emergent adverse events, or TEAEs, during the Correction and Conversion study in **vadadustat Vafseo-** treated patients was 83.8% and 85.5% in darbepoetin alfa treated patients. During the study, the most common TEAEs reported in **vadadustat Vafseo** / darbepoetin alfa treated patients were hypertension **Akebia Therapeutics, Inc. | Form 10-K | Page 68** (16.2% / 12.9%) and diarrhea (10.1% / 9.7%). Serious TEAEs were lower in **vadadustat Vafseo-** treated patients at 49.7% compared to 56.5% for darbepoetin alfa treated patients. The incidence of TEAEs during the prevalent dialysis patient study (Conversion) in the **vadadustat Vafseo-** treated patients was 88.3%, and 89.3% in darbepoetin alfa treated patients. During the study, the most common TEAEs reported in **vadadustat Vafseo** / 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 TEAEs were slightly lower for **vadadustat Vafseo-** 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 PRO2TECT Phase 3 program, the incidence of TEAEs during the erythropoiesis stimulating agent, or-ESA, -untreated patients study (Correction) in the **vadadustat Vafseo** - treated patients was 90.9%, and 91.6% in darbepoetin alfa- treated patients. During the study, the most common TEAEs reported in **vadadustat Vafseo** / 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 TEAEs were 65.3% for **vadadustat Vafseo** - treated patients and 64.5% for darbepoetin alfa- treated patients. The incidence of TEAEs during the ESA- treated patients study (Conversion) in **vadadustat Vafseo-** treated patients was 89.1% and 87.7% in darbepoetin alfa- treated patients. During the study, the most common TEAEs reported in **vadadustat Vafseo** / 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 TEAEs were 58.5% for **vadadustat Vafseo** - treated patients and 56.6% for darbepoetin alfa- treated patients. **For example, during** During the conduct of our Phase 3 program **for Vafseo**, our team and hepatic experts analyzed hepatic cases (unblinded to treatment) and, following the completion of our global Phase 3 clinical program for **vadadustat Vafseo**, there was a review of hepatic safety across the **vadadustat Vafseo** 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 Vafseo** 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, **and these safety concerns were addressed following the FDRR and resubmission to our NDA**. Serious adverse events **considered** related to **vadadustat Vafseo**, including those noted in the CRL **and label**, and any other product candidates could have material adverse consequences on the development and potential **label expansion of Vafseo or the** approval of **vadadustat** or our other product candidates and our business as a whole. Our understanding of adverse events in prior clinical trials of **Vafseo or** 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. **Akebia Therapeutics, Inc. | Form 10-K | Page 70** 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, **Vafseo 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 Vafseo** 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 Vafseo** 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, **Vafseo 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, **Vafseo 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 **vadadustat or any other label expansion for Vafseo or any current or future** 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 U. S. and other jurisdictions. Before obtaining marketing approval for the commercial sale of any product candidate, we must demonstrate through **rigorous and** extensive preclinical **testing development** 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 U. S. and in other jurisdictions, only a small percentage successfully complete the FDA's and other **regulatory** jurisdictions' **Akebia Therapeutics, Inc. | Form 10- K | Page 69** marketing approval processes and are commercialized. Accordingly, even if we are able to obtain the requisite capital to continue to fund our development efforts, we may be unable to successfully obtain regulatory approval for **vadadustat or any other product label expansion or for Vafseo or for any** product candidate, including those that may be in- licensed or acquired. **Further,** We are not permitted to market vadadustat in the U. S. unless and 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 did not support a favorable benefit-risk assessment of vadadustat for dialysis and non-dialysis patients. In October 2022, we submitted the FDRR to the FDA and focused 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 May 2023, the OND denied our appeal but provided a path forward for us to resubmit the NDA for vadadustat for the treatment of anemia due to CKD for dialysis dependent patients without the need for us to generate additional clinical data. In September 2023, we filed our resubmission to our NDA, and in October 2023, the FDA acknowledged that the resubmission was complete and set a PDUFA date of March 27, 2024. There can be no assurances that we will 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. Even if we are able to obtain approval, it will 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 U. S. 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 anemia due to CKD in DD-CKD patients, such approval does not guarantee approval in the U. S. by the FDA for these indications or at all. In addition, while each **Each** regulatory authority makes their own assessment as to the safety and efficacy of a drug, **and the** 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. **In March 2022, we received the CRL from the FDA regarding our NDA for vadadustat for the treatment of anemia due to CKD. Following a FDRR in 2022, we filed a resubmission to our NDA in 2023. On March 27, 2024, the FDA approved our NDA for vadadustat under the trade name Vafseo for the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months. However, we expended significant additional resources to obtain the approval of Vafseo, the approved indication is limited to the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months and the commercialization of Vafseo was delayed, which had and could continue to have an adverse effect on our business. Vafseo is currently approved as a treatment for anemia due to CKD for dialysis dependent patients in the U. S., European Union, United Kingdom, Switzerland and Australia. In Japan, Vafseo is approved as a treatment for anemia due to CKD in both dialysis dependent and non-dialysis dependent patients and is marketed and sold by our collaborator MTPC. In Taiwan and South Korea, Vafseo is approved for the treatment of symptomatic anemia due to CKD in adult patients on chronic maintenance dialysis. We are not permitted to market Vafseo in any additional jurisdictions or other indications until the requisite approval from regulatory authorities in such jurisdiction is received. As a condition to receiving marketing approval for Vafseo in additional territories or for other indications, we may be required by regulatory authorities to conduct additional preclinical studies or clinical trials. For example, we have several lifecycle management and label expansion opportunities currently under evaluation for Vafseo, one of which is the potential for alternative dosing, and another of which is label expansion for the treatment of adult patients with NDD-CKD. However, we may be required to complete additional clinical trials before seeking approval for additional indications, which are time consuming and expensive, and even though Vafseo is approved as a treatment for anemia due to CKD for dialysis dependent patients, we may not be successful in any of our lifecycle management or label expansion opportunities in the timeframe anticipated by us, or at all. For example, we plan to start a Phase 3 trial in the second half of 2025 to potentially expand the Vafseo label to include the treatment of late-stage NDD-CKD patients, however, we may not successfully demonstrate safety and / or efficacy needed to obtain regulatory approval or we may be unable to complete the trial when anticipated or at all. If we do not obtain the approval of label expansion for the treatment of adult patients with NDD-CKD or for alternative dosing in a timely manner, or at all, it could impact future revenue and have an adverse effect on our business.** Obtaining marketing approval in the U. S. 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 / or, 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 (**ferric citrate coordination complex**) 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. In addition April 2024, our partner Akebia Therapeutics, Inc. Form 10-K Page 71 submitted its marketing authorization application for ferric citrate in Europe and the application is still under review. Safety concerns with a given product may impact marketing approval. For example, safety concerns associated with the current standard of care for the indications for Vafseo which we are seeking marketing approval for vadadustat may affect the FDA's or other regulatory authorities' review of the safety results of vadadustat Vafseo. Additionally In addition, 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 our product candidates will never obtain marketing approval in the U. S. or certain other jurisdictions or for some or all of the indications for which we seek approval. For example, changes in or the enactment of additional statutes, promulgation of regulations or issuance of guidance during preclinical or clinical development, or comparable changes in the regulatory review process for each submitted product application, may cause delays in the approval or rejection of an application. 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. Further, on January 31, 2022, the new Clinical Trials Regulation (EU) No 536 / 2014 became applicable in the EU and replaced the prior Clinical Trials Directive 2001 / 20 / EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one EU Member State will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public. We have not previously secured authorization to conduct clinical studies in the EU pursuant to this new regulation and, accordingly, there is a risk that we may be delayed in commencing such studies. The FDA or other regulatory authorities may delay, limit or deny approval of vadadustat any product candidate 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; Akebia Therapeutics, Inc. | Form 10- K | Page 70 • 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 --- label expansion or specifications we request for vadadustat Vafseo; • 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 recent 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 U. S. to support the NDA for potential reasons such as differences in clinical practice from U. S. standards; Akebia Therapeutics, Inc. | Form 10- K | Page 72 • 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 Vafseo 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 Moreover, principal investigators for our future clinical trials may serve as scientific advisors or consultants to us and receive compensation in connection with such services. Under certain circumstances, we experience may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or a comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected

interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates. In addition, we could be adversely affected by several significant administrative law cases decided by the U. S. Supreme Court in 2024. In *Loper Bright Enterprises v. Raimondo*, for example, the court overruled *Chevron U. S. A., Inc. v. Natural Resources Defense Council, Inc.*, which for 40 years required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U. S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the Administrative Procedure Act, or the APA. Additionally, in *Corner Post, Inc. v. Board of Governors of the Federal Reserve System*, the court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, ~~rather~~ rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, *Securities and Exchange Commission v. Jarkesy*, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions could introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays and in obtaining approval of, or if we fail to obtain approval of vadaadustat for some or all of the ~~other impacts~~ indications for which we have sought approval, any of the commercial prospects for vadaadustat may be harmed and our ability to generate revenues will be materially impaired, which could have a material adverse ~~adversely impact~~ effect on our business and operations. **Akebia Therapeutics, Inc. | For Form 10-K | Page 71 Further** example, our resubmission to our NDA for vadaadustat in September 2023 focused on the favorable balance between the benefits and risks of vadaadustat 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 impacted by ongoing litigation challenging the FDA's approval of mifepristone ~~another~~ **company's drug product**. In **Specifically, on April 7, 2023**, the U. S. District Court for the Northern District of Texas **stayed invalidated** the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various ~~conditions~~ **measures** adopted under a REMS. **The** In reaching that decision, the district court made a number of findings that may negatively impact the development, approval and distribution of drug products in the U. S. Among other determinations, the district court held that plaintiffs were likely to prevail in their claim that FDA had acted arbitrarily and capriciously in approving mifepristone without sufficiently considering evidence bearing on whether the drug was safe to use under the conditions identified in its labeling. Further, the district court read the standing requirements governing litigation in federal court as permitting a plaintiff to bring a lawsuit against the FDA in connection with its decision to approve an NDA or establish requirements under a REMS based on a showing that the plaintiff or its members would be harmed to the extent that FDA's drug approval decision effectively compelled the plaintiffs to provide care for patients suffering adverse events caused by a given drug. On April 12, 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 U. S. Supreme Court entered a stay of the district court's decision, in its entirety, pending disposition of the appeal of the district court decision in the Court of Appeals for the Fifth Circuit and the disposition of any petition for a writ of certiorari to the Supreme Court. The Court of Appeals for the Fifth Circuit held oral argument in the case on May 17, 2023 and, on August 16, 2023, issued its decision. The court declined to order the removal of mifepristone from the market **but**, finding that a challenge to the FDA's initial approval in 2000 is barred by the statute of limitations. **But the court did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone that, which the** FDA authorized in 2016 and 2021, were arbitrary and capricious. **In June** On September 8, 2023 **2024**, the Justice Department and a manufacturer of mifepristone filed petitions for a writ of certiorari, requesting that the U. S. Supreme Court review ~~reversed that decision after unanimously finding that the plaintiffs did not have standing to bring this legal action against the FDA.~~ **On October 11, 2024, the Attorneys General of the three states (Missouri, Idaho and Kansas) filed an amended complaint in the U. S. District Court for the Northern District of Texas challenging the FDA's decision actions.** **On December 13-January 16, 2025, the district court agreed to allow these states to file an amended complaint and continue to pursue this challenge.** Depending on the outcome of this litigation, our ability to develop new drug product candidates and to maintain approval of existing drug products could be delayed, undermined or subject to protracted litigation. Finally, with the change in presidential administrations in 2025, there is substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA, CMS and other government agencies with jurisdiction over our products and product candidates. Any change in regulations or policies at FDA, CMS or other government agencies could adversely affect our products and product candidates, including the regulatory process or the pricing or reimbursement of our products or product candidates. In addition, the FDA, CMS and other government agencies recently experienced reductions in workforce and could experience additional such actions. Any disruptions at those agencies or uncertainty from any regulatory changes that affect the development or commercialization of our products and product candidates could present new challenges as we navigate the clinical development and approval process for our product candidates and could have an adverse effect on the commercialization of our products. If we are unable to obtain or maintain marketing approval in jurisdictions outside the United States, we and our partners will not be able to market any product or product candidates outside of the United States. In order to market and sell our product candidates in the European Union, Japan and many other jurisdictions, we or our partners must obtain or maintain separate marketing approvals and

comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The approval procedure varies among countries and can involve additional testing. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The time required to obtain or maintain approval may differ substantially from that required to obtain or maintain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining or maintaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We and our partners may not obtain or maintain approvals from regulatory authorities outside the United States on a timely basis or at all. Additionally, we and our partners could face heightened risks with respect to obtaining or maintaining marketing authorizations in the UK as a result of the withdrawal of the UK from the EU, commonly referred to as Brexit. The UK is no longer part of the European Single Market and EU Customs Union. As of January 1, 2025, the Medicines and Healthcare Products Regulatory Agency, or MHRA, is responsible for approving all medicinal products destined for the United Kingdom market (i. e., Great Britain and Northern Ireland). At the same time, a new international recognition procedure, or IRP, will apply, which intends to facilitate approval of pharmaceutical products in the UK. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators, or RRs. The RRs notably include EMA and regulators in the EEA member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U. S.). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, maintaining or an inability to obtain or maintain, any marketing approvals may force us or our partners to restrict or delay efforts to seek regulatory approval in the UK for our product candidates, which could significantly and materially harm our business. In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023, the U. S. Supreme Court granted The proposed revisions remain to be agreed and adopted by these-- the petitions for writ of certiorari for European Parliament and European Council and the appeals proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry and court-- our business in the long term. Products approved for marketing are subject to extensive post- marketing regulatory requirements, including post- approval pediatric studies for Auryxia and Vafseo, and could be subject to post- marketing restrictions or withdrawal from the Akebia Therapeutics, Inc. | Form 10- K | Page 72 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 and Vafseo, we initially committed to the FDA to conduct certain post- approval pediatric studies of Auryxia and Vafseo under the Pediatric Research Equity Act of 2003, or PREA. Under PREA, an NDA or supplement to an NDA for certain drug products must contain data to assess the safety and effectiveness of the drug product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. 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. We have since been released from the original post marketing requirement, or PMR, and a new PMR was issued that provided that the final report was is due in April 2024. Therefore, this PMR trial is no longer considered delayed and is open and actively enrolling patients. In June 2023 we requested an extension of time for the submission of the final report and such request was denied by the FDA in August 2023. The Therefore, the final report for this PMR trial is still ongoing and actively recruiting patients, but the final report for the trial was due in April 2024, so and we are unlikely to complete the trial is considered delayed by that time. With regard to Auryxia for the treatment of IDA in adult NDD- CKD patients, or 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 required 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 and required that the final report be submitted in August 2024. 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, and we continued to conduct feasibility, however, we have not commenced start- up of this study pending resolution. In February 2024, we requested an extension for the submission of the manufacturing of final report

and such request was denied by the **smaller size tablets** FDA in April 2024. In October 2024, we received a letter from the FDA regarding our non-compliance with PREA due to our failure to complete the IDA post-approval pediatric study, and we submitted our response, including a proposal to waive the PMR with regard to the IDA Indication, to the FDA on November 1, 2024. If the FDA denies our waiver of the PMR with regard to the IDA Indication, or we are unable to complete these studies successfully **by the applicable deadline**, 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 **or other adverse consequences**, 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, **Vafseo 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 contract manufacturing organizations, or 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. 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;** Akebia Therapeutics, Inc. | Form 10-K | Page 73 **trials are complete or that additional safety..... 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 **related to Auryxia or Vafseo** 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 in **the U. S. and Vafseo in the U. S.**, Japan, **Vafseo in Japan and Europe or vadadustat, if approved** in other countries, 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 **Akebia Therapeutics, Inc. | Form 10-K | Page 74** or administrative action, either in the U. S. 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 complex regulatory schemes that require 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 U. S. 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 U. S.; • data privacy laws existing in the U. S., 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, as amended by the California Privacy Rights Act of 2020, or CPRA, as well as other state consumer protection laws, GDPR, any additional applicable EU member state, or 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 **Vafseo 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 Food, Drug and Cosmetic Act of 1938, as amended, or FDCA, which among other things, strictly regulates drug product marketing and promotion and prohibits

manufacturers from marketing such products for off- label use; **Akebia Therapeutics, Inc. | Form 10- K | Page 74** • 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; **Akebia Therapeutics, Inc. | Form 10- K | Page 75** • 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 Open Payments Act (the former Physician Payments Sunshine 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 and specific training 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 **Akebia Therapeutics, Inc. | Form 10- K | Page 75** costs and diversion of management attention and could negatively impact the development, regulatory approval and commercialization of Auryxia or ~~vadadustat~~ **Vafseo**, 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, **Vafseo** 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 U. S. for use in any indications other than the Hyperphosphatemia Indication and the IDA Indication, and **Vafseo for the treatment of anemia due to CKD in adults**

who have been receiving dialysis for at least three months, and all promotional claims must be consistent with the FDA-approved labeling for Auryxia **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. For example, in **January-October 2025-2023**, the FDA published **final-draft** guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This **final-draft** guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use. In addition, under some relatively recent guidance from the FDA and the Pre-Approval Information Securities Exchange Act of 1934, as amended, or **PIE the Exchange Act**, signed into law as part of the Consolidated Appropriations Act of 2023, or the Consolidated Appropriations Act, companies may also **provide-promote** information that is consistent with **the prescribing information** a product's FDA approved labeling 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, and we will need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products. 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** Akebia Therapeutics, Inc. | Form 10-K | Page 76 **Policy changes** 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 **or 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 **disruptions** 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.....** and distraction of management. Disruptions in the FDA, regulatory authorities outside the U. S., **CMS** and other government agencies caused by **funding shortages**, global health concerns or **funding shortages-other events** could prevent **new-products , product candidates** and services from being developed or commercialized in a timely manner, **with expected terms or at all**, which could negatively impact our business. The ability of the FDA and regulatory authorities outside the U. S. to review and approve **new-products and product candidates** can be affected by a variety of factors, including **government budget and funding levels, staffing shortages, statutory, regulatory, and policy changes**, 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 R & D 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. 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. **Akebia Therapeutics, Inc- In addition, with the change in presidential administrations in 2025, there is substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA, CMS and other government agencies with jurisdiction over our products and product candidates.** †
Form 10-K | Page 77 Any change in regulations or policies at FDA, CMS or other government agencies could adversely affect our products and product candidates, including the regulatory process or the pricing or reimbursement of our products or product candidates. In addition, the FDA, CMS and other government agencies recently experienced

reductions in workforce and could experience additional such actions. Any disruptions at those agencies or uncertainty from any regulatory changes that affect the development or commercialization of our products and product candidates could present new challenges as we navigate the clinical development and approval process for our product candidates and could have an adverse effect on the commercialization of our products. These and other actions by the new administration could impact our business as a regulated entity and as a biopharmaceutical company, and we cannot anticipate in what ways and the magnitude of the impacts.

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 UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK 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 the total worldwide annual turnover of a group of companies from the preceding financial year 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 U. S. 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 U. S. There is ongoing uncertainty about the transfer **Akebia Therapeutics, Inc. | Form 10-K | Page 77** 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. Although a new Data Privacy Framework has been adopted, 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. Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. In relation to data transfers, both the UK and the EU have determined, through separate “adequacy” decisions, that data transfers between the two jurisdictions are in compliance with the UK Data Protection Act and the GDPR, respectively. The UK and the U. S. have also agreed to a U. S.-UK “Data Bridge”, which functions similarly to the EU- U. S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the UK to the U. S. In addition to the UK, Switzerland has approved an adequacy decision in relation to the Swiss- U. S. Data Privacy Framework (which would function similarly to the EU- U. S. Data Privacy Framework and the U. S.- UK Data Bridge in relation to data transfers from Switzerland to the U. S.). Any changes or updates to these developments have the potential to impact our business. Additionally, in October 2022, President Biden signed an executive order to implement the EU- U. S. Data Privacy Framework, which serves as a replacement to the EU- U. S. Privacy Shield. The EU initiated the process to adopt an adequacy decision for the EU- U. S. Data Privacy Framework in December 2022, and the EC adopted the adequacy decision on July 10, 2023. The adequacy decision permits U. S. companies who self-certify to the EU- U. S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U. S. However, some privacy advocacy groups have ~~already~~ challenged or suggested that they will be challenging the EU- U. S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU- U. S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business internationally. 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 ~~Akebia Therapeutics, Inc. | Form 10-K | Page 78~~ 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 U. S. 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, or the FTC, and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. For example, the FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be “unfair” under Section 5 of the Federal Trade Commission Act, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The agency is also in the process of developing rules related to commercial surveillance and data security that may impact our business. We will need to account for the FTC’s evolving rules and guidance for proper privacy and data security practices in order to mitigate our risk for a potential enforcement action, which may be costly. If we are subject to a potential FTC enforcement action, we may be subject to a settlement order that requires us to adhere to very specific privacy and data security practices, which may impact our business. We may also be required to pay fines as part of a settlement (depending on the nature of the alleged violations). If we violate any consent order that we reach with the FTC, we may be subject to additional fines and compliance requirements. **New laws**

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. In November 2020, California voters passed a ballot initiative for the CPRA, which went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR- like provisions including requiring that the use, retention and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also creates a new agency that is specifically responsible for enforcing the new law and other California privacy laws. 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 **Akebia Therapeutics, Inc. | Form 10- K | Page 78** 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). In addition to California, at least **eleven** **eighteen** other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of “sensitive” data (which includes health data in some cases). Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the **2023-2024** legislative sessions that will go into effect in 2025 and beyond, including **New Hampshire and New Jersey**. Other states will be considering **these similar** laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, **the State of Washington** state passed a **the My health Health** privacy law **My Data Act** in 2023 that will **which specifically regulate regulated** the collection and sharing of health information **that is not otherwise regulated by the HIPAA rules**, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and **additional more** states (including **Vermont**) are considering such legislation for **2024**. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. **Plaintiffs’ lawyers are** **A broad range of legislative measures** also **increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data- related practices. In particular, there have been introduced a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act. The rise in these types of lawsuits creates potential risk for our business. If we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In recent months, the Officer of Civil Rights, or OCR, has been especially active in enforcing the HIPAA rules. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems. Additionally, OCR is looking to amend the HIPAA Security Rule, which (if and when finalized) could create additional compliance obligations and risk for our business. There are also increased restrictions at the federal level relating to transferring sensitive data outside of the U. S. Accordingly, to certain foreign countries. For example, in 2024, Congress passed H. B. 815, which included the Protecting Americans’ Data from Foreign Adversaries Act of 2024. This law creates certain restrictions for entities that disclose sensitive data (including potential health data) to countries such as China. ~~failure~~ **Failure to comply with current these rules can lead to a potential FTC enforcement action. Additionally, the Department of Justice recently finalized a rule implementing Executive Order 14117, which creates similar restrictions related to the transfer of sensitive US data to countries such as China. These data transfer restrictions (and others that may pass in the future) may create operational challenges and legal risks for our business. 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 future third- party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. 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 could lead to government enforcement actions, private litigation and significant fines and penalties against us, all of which could increase our cost of doing business and have a material adverse effect on our business, financial condition or results of operations. Similarly, failure to comply with federal and state laws regarding privacy and security of personal information could expose us to fines and penalties ~~under such~~. 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, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business. **Further, we cannot assure you that our third- party service providers with access to our or our customers', suppliers', trial patients' and employees' personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations and / or which could in turn adversely affect our business, results of operations and financial condition. We cannot assure you that our contractual measures and our own privacy and security- related safeguards will protect us from the risks associated with the third- party processing, storage and transmission of such information.** **Akebia Therapeutics, Inc. | Form 10- K | Page 79**

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 U. S. or foreign jurisdictions. In the U. S. 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 vadaustat, or any other product candidate, restrict or regulate post- approval activities and affect our ability to profitably sell Auryxia and **Vafseo vadaustat, 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 additional downward pressure on the price that we receive for any FDA approved product, such as Auryxia or **Vafseo vadaustat, if approved**, or any reimbursement that physicians receive for administering any approved product. In the U. S. 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 and regulatory changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2 % per fiscal year, which will remain in effect through 2031. Under current legislation, the actual reductions in Medicare payments may vary up to 4 %. The Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4 % Statutory Pay- As- You- Go Act of 2010 (PAYGO) sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4 % cut to the Medicare program would have taken effect in January 2023. The Consolidated Appropriations Act' s health care offset title includes Section 4163, which extends the 2 % Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031. 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, ~~the U. S. Department of Health and Human Services, or 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 **Vafseo vadaustat, if approved**, or the frequency with which Auryxia and **Vafseo vadaustat, if approved**, is prescribed or used. The costs and prices of prescription pharmaceuticals have also been the subject of considerable discussion in the U. S. 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. In addition, in October 2020, the HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program to import certain prescription drugs from Canada into the U. S. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. **Nine Seven** states (Colorado, Florida, Maine, New Hampshire, New Mexico, ~~North Dakota, Texas, and Vermont and Wisconsin~~) have passed laws allowing for the importation of drugs from Canada. **Certain of North Dakota and Virginia have passed legislation establishing workgroups to examine these-- the impact of a state importation program. As of May 2024, five states (Colorado, Florida, Maine, New Hampshire and New Mexico) have submitted Section 804 Importation Program proposals to the and are awaiting FDA approval. Vermont has submitted a concept letter to HHS.** On January 5, 2023-**2024**, the FDA approved Florida's plan for Canadian drug importation. Further, on July 9, 2021, President Biden signed Executive Order 14063 **Florida now has authority to import certain drugs from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each drug selected for importation, which focuses on, among must be approved by other-- the FDA things, the price of pharmaceuticals. The Order directs HHS state will also need to relabel** create a plan within 45 days to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the **drugs** prices paid by the federal government for such pharmaceuticals, and **perform quality testing** to address the recurrent problem of price gouging **the products to meet FDA standards**." On September 9, 2021, HHS released its Akebia Therapeutics, Inc. | Form 10- K | Page 80 As an oral drug, **Auryxia was covered by Medicare under Part D until January 1, 2025. In January 2011, CMS implemented the ESRD PPS, a prospective payment system for dialysis treatment. Under the ESRD PPS, CMS generally makes a single bundled payment to the dialysis facility for each dialysis treatment that covers all items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare-certified ESRD facilities or at their home. As of January 2025, oral ESRD-related drugs without injectable or intravenous equivalents, including Auryxia and all other phosphate lowering medications, are included in the ESRD bundle and separate Medicare payment for these drugs are no longer available, but ESRD facilities will receive a TDAPA for Auryxia for a period of at least two years starting on January 1, 2025. Vafseo, which we began selling in January 2025, is also included in the ESRD bundle and ESRD facilities will receive a TDAPA for Vafseo as a new renal dialysis drug meeting certain criteria for a period of at least two years starting on January 1, 2025. The TDAPA provides separate payment based on the drug's ASP that will be in addition to the base rate in order to facilitate the adoption of innovative therapies. If the TDAPA reimbursement amount for Auryxia or Vafseo is lower than anticipated, or if TDAPA is eliminated, it would have an adverse impact on our revenue. Additionally, in the post-TDAPA period, CMS currently expects to increase the single bundled payment base rate paid to the dialysis facility for each dialysis treatment to reflect that bundled drugs will be reimbursed as part of the single bundled payment for Medicare patients. However, there can be no assurances that any increase in the single bundled payment base rate will be sufficient to adequately reimburse the dialysis facilities for Auryxia or Vafseo at a price that allows us to continue to sell Auryxia or Vafseo at a profit. In July 2024, Ardelyx filed a complaint in the United States District Court for the District of Columbia against HHS, CMS and other parties, which alleged that CMS's plan to include oral-only phosphate lowering therapies in the ESRD PPS violated its statutory and regulatory authority under the Medicare Improvements for Patients and Providers Act, which established the ESRD PPS bundled payment system for dialysis services. In October 2024, Ardelyx filed a motion for a preliminary injunction to enjoin CMS from including oral-only phosphate lowering therapies in the ESRD PPS. CMS had earlier filed a motion to dismiss the complaint on jurisdictional grounds. On November 8, 2024, the district court denied Ardelyx's motion for a preliminary injunction and it granted the government's motion to dismiss. Thereafter, Ardelyx moved for reconsideration, but the district court also denied that request. On December 26, 2024, Ardelyx filed a notice of appeal with the US Court of Appeals for the DC Circuit. If Ardelyx is successful in its claims, oral-only phosphate lowering therapies, including Auryxia, may be removed from the ESRD bundle, which could reduce anticipated revenue pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for **Auryxia** 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. 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 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. We consider many factors when we implement a price increase for a product, including historical and potential future inflation rates. However, there are many variables that are outside of our control and if we increase the price of Auryxia or **Vafseo vadadustat, if approved,** faster than the pace of inflation, we would be subject to additional rebates under Medicare, which could have a material adverse effect on**

our product revenues. As an oral drug, Auryxia is covered by Medicare under Part D. In January 2011, CMS implemented the ESRD PPS, a prospective payment system for dialysis treatment. Under the ESRD PPS, CMS generally makes a single bundled payment to the dialysis facility for each dialysis treatment that covers all items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare-certified ESRD facilities or at their home. The inclusion of oral medications without injectable or intravenous equivalents such as Auryxia in the bundled payment was initially delayed by CMS until January 1, 2014, and through several subsequent legislative actions has been delayed until January 1, 2025. Absent further legislation or regulation on this matter, beginning in January 2025, oral ESRD-related drugs without injectable or intravenous equivalents, including Auryxia and all other phosphate lowering medications, will be included in the ESRD bundle and separate Medicare payment for these drugs will no longer be available, as is the case today under Medicare Part D. ESRD facilities may nonetheless receive a TDAPA for new renal dialysis drugs and biological products that meet certain criteria for a period of two years. The TDAPA will provide separate payment based on the drug's ASP that will be in addition to the base rate in order to facilitate the adoption of innovative therapies. There can be no assurances that CMS will determine that Auryxia will qualify for TDAPA status or that CMS will not again delay the inclusion of these oral ESRD-related drugs in the bundled payment. Even if Auryxia is deemed eligible by CMS, revenue for sales of Auryxia could be significantly less in the TDAPA period than it would be if Auryxia is not bundled into the ESRD PPS. Moreover, in the post-TDAPA period, CMS currently expects to increase the single bundled payment base rate paid to the dialysis facility for each dialysis treatment to reflect that oral only phosphate lowering drugs will be reimbursed as part of the single bundled payment for Medicare patients. There can be no assurances that any increase in the single bundled payment base rate will be sufficient to adequately reimburse the dialysis facilities for Auryxia at a price that is profitable for us. Specifically, with **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. **On August 15, 2024, HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, CKD and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. Subsequently, on January 17, 2025, HHS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations. This second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027. CMS issued a public statement on January 29, 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program.** 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 \$ 4-2,000 a year in 2024 and, thereafter beginning in 2025, at \$ 2,000 a year. On June 6, 2023, Merck & Co. Inc., or Merck, filed a lawsuit against HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the **Akebia Therapeutics, Inc. | Form 10-K | Page 81** Constitution. Subsequently, a number of other parties, including the U. S. Chamber of Commerce, ~~the Chamber~~, Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against HHS and CMS. **There have been various decisions by the courts considering these cases since they were filed. The HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases.** We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results. Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition. **Akebia Therapeutics, Inc. | Form 10-K | Page 81** 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 U. S. 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 **or Vafseo** 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, **Vafseo** and any ~~products-~~ **product** 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, **Vafseo** 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 EU Member States, 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 EU 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. Our reporting and payment obligations under the Medicaid Drug Rebate Program, **Medicare** and other governmental drug pricing programs are complex and may involve subjective decisions. Any failure to properly comply with those obligations could subject us to penalties and sanctions. As a condition of reimbursement by various federal and state health insurance programs, we are required to calculate and report certain pricing information to federal and state agencies. The regulations governing the calculations, price reporting and payment obligations are complex and subject to interpretation by various government and regulatory agencies, as well as **Akebia Therapeutics, Inc. | Form 10- K | Page 82** the courts. Reasonable assumptions have been made where there is lack of regulations or clear guidance and such assumptions involve subjective decisions and estimates. We are required to report any revisions to our calculation, price reporting and payment obligations previously reported or paid. Such revisions could affect our liability to federal and state payors and also adversely impact our reported financial results of operations in the period of such restatement. Further, a number of states have either implemented or are considering implementation of drug price transparency legislation that may prevent or limit our ability to take price increases at certain rates or frequencies. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers for the untimely, inaccurate, or incomplete reporting of drug pricing information or for otherwise failing to comply with drug price transparency **Akebia Therapeutics, Inc. | Form 10- K | Page 82** requirements. If we are found to have violated state law requirements, we may become subject to significant penalties or other enforcement mechanisms, which could have a material adverse effect on our business. Uncertainty exists as new laws, regulations, judicial decisions, or new interpretations of existing laws, or regulations related to our calculations, price reporting or payments obligations increases the chances of a legal challenge, restatement or investigation. If we become subject to investigations, restatements, or other inquiries concerning our compliance with price reporting laws and regulations, we could be required to pay or be subject to additional reimbursements, penalties, sanctions or fines, which could have a material adverse effect on our business, financial condition and results of operations. In addition, it is possible that future healthcare reform measures could be adopted, which could result in changes to how we calculate or report certain pricing information to federal and state agencies, or increased pressure on pricing and reimbursement of our products and thus have an adverse impact on our financial position or business operations. Further, state Medicaid programs may be slow to invoice pharmaceutical companies for calculated rebates resulting in a lag between the time a sale is recorded and the time the rebate is paid. This results in us having to carry a liability on our consolidated balance ~~sheets-~~ **sheet** for the estimate of rebate claims expected for Medicaid patients. If actual claims are higher than current estimates, our financial position and results of operations could be adversely affected. In addition to retroactive rebates and the potential for 340B Program refunds, if we are found to have knowingly submitted any false price information related to the Medicaid Drug Rebate Program to CMS, we may be liable for civil monetary penalties. Such failure could also be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program. In the event that CMS terminates our rebate agreement, federal payments may not be available under government programs, including Medicaid or Medicare Part B, for our covered outpatient drugs. Additionally, if we overcharge the government in connection with the Federal Supply Schedule pricing program or Tricare Retail Pharmacy Program, whether due to a misstated Federal Ceiling Price or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and / or to identify contract overcharges can result in allegations against us under the FDCA and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time- consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Our collaborators are also subject to similar requirements outside of the U. S. and thus the attendant risks and uncertainties. If our collaborators suffer material and adverse effects from such risks and uncertainties, our rights and benefits for our licensed products could be negatively impacted,

which could have a material and adverse impact on our revenues. With the passage of the CREATES Act, we are exposed to possible litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market- based terms for testing in support of their ~~abbreviated new drug applications, or~~ ANDAs, 505 (b) (2) NDAs and biosimilar product applications. In December 2019, ~~former~~ President Trump signed legislation intended to facilitate the development of generic and biosimilar products. The bill, previously known as the CREATES Act, authorizes sponsors of ANDAs, 505 (b) (2) NDAs or biosimilar product applications to file lawsuits against companies holding NDAs or BLAs that decline to provide sufficient quantities of an approved reference drug or biological product on commercially reasonable, market- based terms. Drug or biological products on FDA’s drug shortage list are exempt from these new provisions unless the product has been on the list for more than six continuous months or the FDA determines that the supply of the product will help alleviate or prevent a shortage. To bring an action under the statute, the developer of a product candidate that seeks to develop the product and seek approval under an ANDA, 505 (b) (2) NDA, or biosimilar product application must take certain steps to request the reference product from the reference product manufacturer, which, in the case of products covered by a REMS with elements to assure safe use, include obtaining authorization from the FDA for the acquisition of the reference product. If the reference product manufacturer does not provide the reference product and the ANDA, 505 (b) (2) NDA, or biosimilar product sponsor does bring an action for failure to provide a reference product, there are certain affirmative defenses available to the reference product manufacturer, which must be shown by a preponderance of evidence, including that the NDA or BLA holder sells the **Akebia Therapeutics, Inc. | Form 10- K | Page 83** reference product through agents, distributors, or wholesalers and has placed no restrictions, explicit or implicit, on selling the reference product to ANDA, 505 (b) (2) or biosimilar sponsors. If the sponsor prevails in litigation, it is entitled to a court order directing the reference product manufacturer to provide, without delay, sufficient quantities of the applicable product on commercially reasonable, market-based terms, plus reasonable attorney fees and costs. Additionally, the new statutory provisions authorize a federal court to award the product developer an amount “ sufficient to deter ” the reference product manufacturer from refusing to provide sufficient product quantities on commercially reasonable, market- based terms, up to a certain maximum amount based on revenue earned while in noncompliance, if the court finds, by a preponderance of the evidence, that the reference product manufacturer did not have a legitimate business justification to delay providing the product or failed to comply with the court’s order. For the purposes of the statute, the **Akebia Therapeutics, Inc. | Form 10- K | Page 83** term “ commercially reasonable, market- based terms ” is defined as (1) the nondiscriminatory price at or below the most recent wholesale acquisition cost for the product, (2) a delivery schedule that meets the statutorily defined timetable, and (3) no additional conditions on the sale. Although we intend to comply fully with the terms of these statutory provisions, we are still exposed to potential litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market- based terms for testing in support of ANDAs, 505 (b) (2) NDA applications or biosimilar product applications. Such litigation would subject us to additional litigation costs, damages and reputational harm, which could lead to lower revenues. The CREATES Act may facilitate future competition with Auryxia **or Vafseo** and any of our product candidates, if approved, which could impact our ability to maximize product revenue. 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, **including an authorized generic version of Auryxia, Riona, and 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, and 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 Vafseo** in Japan and certain other Asian countries. In addition, we ~~entered into the Vifor Agreement pursuant to which we granted CSL Vifor an exclusive license to sell vadadustat to the Supply Group in the U. S. We also granted to Averoa an exclusive license to develop and commercialize ferric citrate in the Averoa Territory EEA, Turkey, Switzerland and the United Kingdom. Furthermore, in May 2023, we entered into a license agreement with Medice, pursuant to which we granted Medice an exclusive license to develop and commercialize vadadustat Vafseo for the treatment of anemia in patients with CKD chronic kidney disease~~ entered into a license agreement with Medice, pursuant to which we granted Medice an exclusive license to develop and commercialize **vadadustat Vafseo** for the treatment of anemia in patients with **CKD chronic kidney disease** in the Medice Territory. 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 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 Pharmaceutical Co. Ltd., or Otsuka, elected to terminate our collaboration agreements with them, and we subsequently negotiated a Termination and Settlement Agreement with Otsuka. This termination by Otsuka may have delayed the launch of ~~vadadustat~~ **Vafseo** in Europe or other territories previously licensed to Otsuka or adversely ~~affected~~ **affected** how we are perceived in scientific and financial communities. For example, in August 2023, Medice informed us that their launch of Vafseo in certain countries in the Medice Territory was going to be later than previously anticipated due to the activities required to enable the launch. If we are unable to maintain our collaborations, we may not be able to capitalize on the market potential of our products or product candidates, and our business could be materially harmed. 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; Akebia Therapeutics, Inc. | Form 10- K | Page 84 **collaborations, we may not be able to capitalize on the market potential of our products or product candidates, and our business could be materially harmed. In February 2025, in advance of the potential market entry of generic competition to our branded Auryxia on or after March 20, 2025, we entered into an Authorized Generic Distribution and Supply Agreement with our AG Partner, pursuant to which, on or after March 20, 2025, our AG Partner will sell an authorized generic version of Auryxia. We will be relying on our AG Partner for the commercialization of this authorized generic. If competition, including from generics other than our AG Partner, capture sales or if generics are sold at a greater discount to Auryxia's price than anticipated, it could materially and adversely affect our expected revenues. In addition, we are responsible for supplying product to our AG Partner, and if there are problems in the supply chain, we could be subject to certain penalties, which could be substantial. 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 ~~or~~ 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; • inefficiencies or structural changes in internal operations or processes of our collaborators may lead to increased expenses associated with commercializing a product, including manufacturing costs, rebates, **product** returns and other adjustments which would negatively impact net product revenue; • 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 occur, the market potential of Auryxia, **including our authorized generic, Riona ~~or~~ 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 may decide to enter into additional collaborations for the development and commercialization of Auryxia, **Vafseo** or our product candidates, ~~including vadadustat~~, both within and outside of the U. S. For example, in May 2023, we entered into the license agreement with Medice, pursuant to which we granted Medice an exclusive license to develop and commercialize ~~vadadustat~~ **Vafseo** for the treatment of anemia in patients with **CKD chronic kidney disease** in the Medice Territory. Any of these relationships may require us to incur non- recurring **and** other charges, increase our near..... collaborator's resources and expertise; and Akebia Therapeutics, Inc. | Form 10- K | Page 85 **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 U.S.; • a potential collaborator's evaluation of Auryxia, **Vafseo 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, **Vafseo** or the development and potential commercialization of any of our product candidates, ~~including vadadustat, if approved~~, reduce or delay our development programs, or increase our expenditures and undertake additional development or commercialization activities at our own expense. ~~For example, following the termination of our collaboration agreements with Otsuka in 2022, we incurred additional expenses in connection with the development of vadadustat in Europe and other countries~~. 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, **Vafseo** or our other product candidates. **For example, including vadadustat following the termination of our collaboration agreements with Otsuka in 2022, if approved we incurred additional expenses in connection with the development of Vafseo in Europe and other countries**. 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 **Vafseo** 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 were eligible to receive up to an additional \$ 5. 0 million in each year from 2021 through 2023 under the Royalty Agreement if specified sales milestones were achieved for vadadustat in the territory covered by the MTPC Agreement, subject to the satisfaction of certain customary conditions, and we did not achieve such milestones~~. 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 **Vafseo** in the territory covered by the MTPC Agreement. Negative fluctuations in these royalty revenues could delay, diminish or eliminate 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 commercial distribution, and in many instances only have a single supplier or distributor, and the loss of these manufacturers or distributors, 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 products 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. We also utilize third parties for the commercial distribution of Auryxia **and Vafseo**, including wholesale distributors and certain specialty pharmacy providers. 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 or distribute sufficient quantities of Auryxia **and vadadustat, Vafseo or any of our product candidates** 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 **suppliers** for each of Auryxia drug substance and drug product, **including our authorized generic, and vadadustat Vafseo** drug substance and drug product, and alternate sources of supply may not be readily available. We have **also engaged Cardinal Health, Inc..... for Auryxia or vadadustat are terminated;** Akebia Therapeutics, Inc. | Form 10- K | Page 86 **also engaged Cardinal Health, Inc.**, as the exclusive third- party logistics distribution agent for commercial sales of Auryxia **and Vafseo**. If any of the following occurs, we may not have sufficient quantities of Auryxia, **Vafseo and / or vadadustat** our product candidates 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 Vafseo 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 due to technical issues, natural disasters or other reasons, 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; • 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; or • any of our third party distributors fail to perform or encounter any damage or other disruption at their facilities. If we, or any of our third party manufacturers or distributors cannot or do not perform as agreed or expected, or any of our customers were to experience further shutdowns, delays or other business disruptions, including as a result of catastrophic events, including pandemics, 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 or distribute the materials ourselves, for which we currently do not have the capabilities or resources, or enter into agreements with other third party manufacturers or distributors, which we may not be able to do in a timely manner or on favorable or reasonable terms, if at all. If any of these events occur, especially with respect to one of our sole source suppliers, we may not have sufficient quantities of product for the commercialization of Auryxia and / or **Vafseo vadadustat, if approved**, or may experience delays in the development of our products or product candidates, which could materially and adversely impact our business and results of operation. **In addition, if we do not have sufficient**

quantities of Auryxia, including our authorized generic, For – or example, one Vafseo to satisfy the requirements of our manufacturers has notified us that it will customer and supply contracts, we may be subject to penalties, which could discontinuing operations at one site at a future date and then we will only be substantial able to manufacture at their other site. 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 Vafseo. 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 Vafseo, where approved, in a timely manner, within budget, or at all. In addition, the cost of obtaining Auryxia and vadadustat Vafseo 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 Vafseo, including the costs of raw materials, and have seen increases in the production costs of Auryxia and vadadustat Vafseo, and any significant increase in the cost of obtaining our products could materially adversely affect our revenue for Auryxia and Vafseo 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 for new products or affect commercial supply of Auryxia or Vafseo 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 our 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 had experienced issues in manufacturing Auryxia, and if we continue to experience manufacturing issues going forward, or incur additional costs, 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 Vafseo 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 Vafseo 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..... the manufacture of certain starting materials, Akebia Therapeutics, Inc. | Form 10- K | Page 87 processes used by our third party manufacturers to manufacture Auryxia and Vafseo 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 Vafseo 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 – or vadadustat Vafseo, 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, if 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 high amounts of write- downs to inventory reserves in the future, it could negatively impact our ability to supply Auryxia or Vafseo, and our financial condition could be harmed. If the FDA or other regulatory authorities do not approve the facilities being used to manufacture vadadustat, or if the EMA or other regulatory authorities withdraws any approval of the facilities being used to manufacture Auryxia, and / or Vafseo or any of our product candidates, we may need to find alternative manufacturing facilities, which would significantly impact our ability to continue commercializing Auryxia or Vafseo in Japan, or to commercialize Vafseo in Europe and other countries, or to develop, obtain marketing approval for or market Vafseo vadadustat or our other product candidates, if approved. Moreover, our failure or the failure of our third party manufacturers or distributors 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 or

distributors, 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 **the U. S., Japan or Europe**, 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~~ **Vafseo**. 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, ~~or Vafseo in Japan, Europe or other countries or~~ ~~vadadustat, if approved in other countries,~~ 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' or distributors' control, it may adversely impact our ability to supply Auryxia or ~~vadadustat~~ **Vafseo**, and we may incur significant financial harm. In addition, Auryxia, Vafseo and ~~vadadustat~~ **our product candidates** may compete with other products and product candidates for access to third party manufacturing facilities. A third party manufacturer or distributor may also encounter delays or operational issues brought on by sudden internal resource constraints, labor disputes, shifting priorities or shifting regulatory protocols. Certain of these third party manufacturing facilities may be contractually prohibited from manufacturing Auryxia, Vafseo or ~~vadadustat~~ **our product candidates** due to exclusivity provisions in agreements with our competitors. Any of the foregoing could negatively impact our third party manufacturers' or distributors' ability to meet our demand, which could adversely impact our ability to supply Auryxia, Vafseo or ~~vadadustat~~ **our product candidates**, and we may incur significant financial harm. Our current and anticipated future dependence on third parties for the manufacture and distribution of Auryxia, Vafseo and ~~vadadustat~~ **our product candidates** may adversely affect our and our partners' ability to commercialize Auryxia, Vafseo and ~~vadadustat~~ **our product candidates**, 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~~ **Vafseo** 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 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~~ **Auryxia or Vafseo, or failing to obtain or maintain marketing approval or for** 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~~ **Auryxia**, **Vafseo** 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 U. S. 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, 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 us in writing that Panion would terminate the Panion License Agreement on November 21, 2018 if we did not cure the breach alleged by Panion, specifically, that we failed to use commercially reasonable best efforts to commercialize Auryxia outside the U. S. We 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 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 U. S. 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 10, Commitments and Contingencies, to our consolidated financial statements in Part II, Item 8. Financial Statements of this Form 10-K 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.

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.

Changes in U. S. and international trade policies, particularly with respect to China or Canada, may adversely impact our business and operating results. The U. S. government has recently made statements and taken certain actions that may lead to potential changes to U. S. and international trade policies, including imposing several rounds of tariffs and export control restrictions affecting certain products manufactured in China, Canada and potentially other countries. In March 2018, the Trump administration announced the imposition of tariffs on steel and aluminum entering the U. S. from China, and in June 2018, the Trump administration announced further tariffs targeting goods imported from China. Recently both China and the U. S. have each imposed tariffs indicating the potential for further trade barriers, including the U. S. Commerce Department adding numerous Chinese entities to its "unverified list," which requires U. S. exporters to go through more procedures before exporting goods to such entities. In March 2025, the U. S. imposed tariffs on certain imports from Canada and Mexico. However, these newly imposed tariffs have resulted in retaliatory tariffs, and threats thereof, against U. S. goods. It is unknown whether and to what extent new tariffs, export controls, or other new laws or regulations will be adopted, or the effect that any such actions would have on us or our industry. Further, many of our manufacturers and suppliers for Auryxia and Vafseo are located in China and Canada. The manufacturing of our drug product for commercial use of both Auryxia and Vafseo takes place in Canada through a third-party manufacturer, Patheon Inc., or Patheon. Also, the manufacturing of our drug substance and drug product for commercial supply of Vafseo takes place in China through a third-party manufacturer, STA Pharmaceutical Hong Kong Limited, a subsidiary of WuXi AppTec, or WuXi STA, and we will likely continue to rely on foreign CMOs in the future. We also rely on third parties in China for the supply of raw materials used in the manufacture of Vafseo and for certain early-stage research services. Trade tensions and conflicts between the U. S. and China, Canada or other countries have recently been escalating and, as such, we are exposed to the possibility of product supply disruption and increased costs and expenses in the event of changes to the laws, rules, regulations and policies of the governments of the U. S., China, Canada or other countries, or due to geopolitical unrest and unstable economic conditions. In addition, certain Chinese biotechnology companies may become subject to trade restrictions, sanctions, other regulatory requirements or proposed legislation by the U. S. government, which could restrict or even prohibit our ability to work with such entities, thereby potentially disrupting their supply of material to us. For example, in February 2024, U. S. lawmakers called for investigations into and the imposition of possible economic sanctions against Chinese biotechnology companies WuXi AppTec and WuXi Biologics, or collectively WuXi, over alleged ties to the Chinese military. Further, the recently proposed BIOSECURE Act introduced in the House of Representatives, as well as a substantially similar bill in the Senate, targets certain Chinese biotechnology companies. If these bills become law, or similar laws are passed, they would have the potential to severely restrict the ability of companies to contract with certain Chinese biotechnology companies of concern without losing the ability to contract with, or otherwise receive funding from, the U. S. government. Such disruptions could have adverse effects on our ability to commercialize Vafseo or the development of our product candidates and our business operations. Any unfavorable government policies on international trade, such as export controls, capital controls or tariffs, may increase the cost of manufacturing our products and product candidates, affect the demand for our products, the competitive position of our products or product candidates, and

import or export of raw materials and finished product candidate used in our preclinical studies and clinical trials, particularly with respect to any product candidates and materials that we import from China and Canada, including pursuant to our manufacturing service arrangements with WuXi STA and Patheon. If any new tariffs, export controls, legislation and / or regulations are implemented, or if existing trade agreements are renegotiated or, in particular, if either the U. S., Chinese, Canadian or other government takes retaliatory trade actions due to the recent trade tension, such changes could have an adverse effect on our business, financial condition and results of operations. 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 **Akebia Therapeutics, Inc. | Form 10-K | Page 90** seek to protect our proprietary products and technology by filing patent applications in the U. S. 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-products** 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-products**. 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 U. S. 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-products** and technologies which may have an adverse effect on our business. If our competitors prepare and file patent applications in the U. S. 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 U. S., 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 U. S. 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 U. S., 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 U. S. 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 U. S. or elsewhere, challenging our patent rights or the patent rights of others. An adverse result in any such proceeding or litigation could reduce **Akebia Therapeutics, Inc. | Form 10-K | Page 90** 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 U. S. 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 **Akebia Therapeutics, Inc. | Form 10-K | Page 91** 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 U. S. may be less extensive than those in the U. S. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the U. S. As a result, we may not be able to prevent third parties from practicing our inventions in all countries outside the U. S., or from selling or importing products made using our inventions in and into the U. S. 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 U. S. 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 U. S. 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, **Vafseo vadadustat, if approved,** or other future products. The patent rights and related non- patent exclusivity that we own or have licensed relating to Auryxia, **Vafseo vadadustat,** or other future products, are, or may be limited in ways that may affect our ability to exclude third parties from competing against us. **Akebia Therapeutics, Inc. | Form 10- K | Page 91** 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 or our partners from marketing and selling Auryxia, Vafseo or **vadadustat, if approved, or** other future products, increase the risk that a generic or other similar version of Auryxia, Vafseo or **vadadustat, if approved, or** other future products could enter the market to compete with Auryxia, Vafseo or **vadadustat, if approved, or** other future products, limit our or our partners' development and commercialization of Auryxia, Vafseo or **vadadustat, if approved, or** other future products, or otherwise harm our competitive position and result in additional significant costs. **Akebia Therapeutics, Inc. | Form 10- K | Page 92** 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 U. S., we may seek non- patent exclusivity for **vadadustat and other any approved or** future products 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 future** products will receive such exclusivity. The FDCA provides a five- year period of non- patent exclusivity within the U. S. 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) **! Vafseo was granted NCE status following its approval in March 2024 and received a five- year NCE exclusivity** . 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 U. S., the FDA has the authority to grant additional regulatory exclusivity protection for approved drugs where the sponsor conducts specified testing in pediatric or adolescent populations. If granted, this pediatric exclusivity may provide an additional six months which are added to the term of any non-patent exclusivity that has been awarded as well as to the regulatory protection related to the term of a relevant patent, to the extent these protections have not already expired. **In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted regarding non-patent exclusivity. For example, EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the EC in November 2020. The EC's proposal for revision of several legislative instruments related to medicinal products, which may reduce the duration of regulatory data protection and exclusivity periods for orphan drugs, and revise the eligibility for expedited pathways in addition to other changes, was published on April 26, 2023. On April 10, 2024, the European Parliament adopted a position on the proposal requesting several amendments to the package. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry and our business in the long term.** We cannot assure you that Auryxia, ~~Vafseo vadadustat, if approved,~~ or any of our potential future products will obtain such pediatric exclusivity, NCE exclusivity or any other market exclusivity in the U. S., 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 ~~Akebia Therapeutics, Inc. | Form 10-K | Page 92~~ also cannot assure you that Auryxia, ~~Vafseo vadadustat, if approved,~~ or any of our potential future products will obtain patent term extension. **Akebia Therapeutics, Inc. | Form 10-K | Page 93** 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 **and Vafseo** sales and have an adverse impact on our business and results of operation. Although the composition and use of Auryxia is currently claimed by ~~143~~ issued patents that are listed in the FDA's Orange Book, **or OB, and the composition and use of Vafseo is currently claimed by 13 issued patents that are listed in the OB**, 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, **Vafseo** 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 **or Vafseo** is approved and launched sooner than we anticipate, revenue from Auryxia **or Vafseo, respectively**, 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 U. S. 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. **While we expect that the availability of generic versions of Auryxia will negatively impact our net product revenue for Auryxia and our results of operations, it is difficult to estimate the impact of generics on Auryxia net product revenue, and if the impact is greater than we currently anticipate, it may materially adversely impact our business and results of operations.** 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 U. S. 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, vada~~du~~stat Vafseo 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 product 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 U. S. 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 U. S. or import into the U. S. 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 two~~ commercial product ~~products~~ ; Auryxia . We received the CRL from the FDA regarding our NDA for vada~~du~~stat in March 2022, and Vafseo we resubmitted our NDA in September 2023. If in the future vada~~du~~stat is approved, vada~~du~~stat could be commercialized. We attempt to ensure that our products and product candidates and the methods we employ to Akebia Therapeutics, Inc. | Form 10-K | Page 93-94 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 U. S. 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. In November 2023, we and our collaboration partner, MTPC, entered into a Settlement and Cross License Agreement, or the Settlement Agreement, with FibroGen and its collaboration partner, Astellas. The Settlement Agreement resolves all patent disputes between us, MTPC, FibroGen and Astellas in the EU, the contracting states to the European Patent Convention, the UK and Japan, or the Settlement Territory. We discuss the status of the opposition and proceedings against certain FibroGen patents in Part I, Item 3. Legal Proceedings of this Form 10-K. We may in the future initiate invalidity actions or other legal proceedings with respect to FibroGen patents outside of the Settlement Territory. If we are not successful in such proceedings, FibroGen could try to claim that our products infringe their patent rights. Third parties, including FibroGen, may in the future claim that our ~~product products~~ and product candidates and other technologies infringe upon their patents and may challenge our ability to commercialize Auryxia and Vafseo vada~~du~~stat, 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 Vafseo or further develop and commercialize vada~~du~~stat 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 proceedings in the **Indian Patent Office and the European Patent Office and Indian Patent Office**. These ~~proceedings~~ **The** proceedings may be ongoing for a number of years, **may be resolved in a manner adverse to the Company** and may involve substantial expense and diversion of employee resources from **our business, which could have an adverse effect on** 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”. Akebia Therapeutics, Inc. | Form 10-K | Page **94**

95 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~~ **obtain and /or maintain marketing approval of and commercialize Auryxia, Vafseo or any of our product candidates**, recruit and retain qualified personnel is critical to our success. We are also highly dependent on our executives, certain members of our senior management and certain **key personnel** 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, we implemented a reduction of our workforce in April and May 2022 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 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 Vafseo and other any~~ **obtain and /or maintain marketing approval of and commercialize Auryxia, vadadustat Vafseo and other any** product candidates. Our future financial performance and our ability to develop, ~~obtain and /or maintain marketing approval of and commercialize Auryxia and vadadustat Vafseo~~ **obtain and /or maintain marketing approval of and commercialize Auryxia and vadadustat Vafseo** 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 for our personnel from our competitors and other companies throughout our industry, particularly in our geographic region. Over the last several years, the challenges in recruiting and retaining employees across the pharmaceutical and biotechnology industries have increased substantially due to current industry job market dynamics. In addition, we rely on contractors, consultants and advisors, including scientific and clinical advisors, to assist us in formulating and executing our R & D 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 we implemented a reduction in workforce in April and May 2022 by approximately 42% across all areas of our Company, including several members of management. In November 2022, we also implemented a reduction of Akebia Therapeutics, Inc. | Form 10-K | Page 95 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. The reductions in workforce reflected our determination to refocus our strategic priorities around our commercial product, Auryxia, and our development portfolio, and were steps in a broader cost savings plan to significantly reduce our operating expense profile. 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 \$ 0.2 million and \$ 15.9 million in the years ended December 31, 2023 and 2022, 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 NDA resubmission 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 U. S., we will need to hire additional employees to support the commercialization of vadadustat in the U. S., 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 partnerships and 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 **in Japan, the development and commercialization of ferric citrate in Europe,** and the development and commercialization of vadadustat, which is now being or will be marketed under the trade name Vafseo by our collaboration partner, MTPC, in Japan and **potentially other Asian countries and** our collaboration partner, Medice, in the Medice Territory. **Additionally, in the U. S., we have a strategic relationship with CSL Vifor related to the commercialization of vadadustat, if approved.** As our operations continue, **Akebia Therapeutics, Inc. | Form 10-K | Page 96** we expect that we will need to manage our current relationships and enter into new relationships 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. For example, we supply or have agreed to supply, as applicable, Auryxia in Europe, Vafseo in Japan, Europe and other territories where it is approved, **and vadadustat in the U. S., if approved,** for commercial and clinical use to MTPC, Medice, **and** Averoa **and** CSL Vifor, which will require us to successfully manage our limited financial and managerial resources. In addition, we may not be able to obtain the raw materials or product that we need, or the cost of the raw materials or product may be higher than expected. If we are unable to successfully manage our supply obligations, our ability to commercialize our products or supply such products to our partners could have a material adverse effect on our relationships with our partners and our results of operations. Our future financial performance and our ability to commercialize Auryxia and **vadadustat Vafseo**, 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. **For example, we recently transitioned to a new enterprise resource planning system and if we encounter any difficulties or issues with the new system it could affect our ability to close our books and complete our financial reporting in a timely manner.** 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. We have identified a material weakness in our internal control over financial reporting as of December 31, **2023-2024** relating to our accounting for inventory and inventory related transactions. If we are not able to remediate this material weakness, or **Akebia Therapeutics, Inc. | Form 10-K | Page 96** if we experience additional material weaknesses or other deficiencies in our internal control over financial reporting in the future or otherwise fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately or timely report our financial results or prevent fraud, and we may conclude that our internal control over financial reporting is not effective, which may

adversely affect our business. Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to maintain or implement required new or improved controls, or difficulties encountered in implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us, as and when required, conducted in connection with Section 404 of the Sarbanes-Oxley Act, or Section 404, or any testing by our independent registered public accounting firm may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. We identified a material weakness in our internal control over financial reporting as of December 31, 2023-2024. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements will not be prevented or detected on a timely basis. ~~Our~~ Specifically, our management concluded that we did not design and maintain effective controls over **inventory. Specifically, we did not maintain effective review controls that operated with a sufficient level of precision to evaluate the completeness and accuracy and reasonableness of accounting for the product sales forecast, which is used in the evaluation of excess inventory and inventory-related transactions, including the inventory reconciliations, calculation of excess overheads, presentation of inventory in our balance sheet between short-term and long-term and our liabilities related to the calculation of firm purchase commitments and the classification of current and non-current inventory.** For further discussion of the material weakness, see Part II, Item 9A, "Controls and Procedures." We have taken ~~certain steps~~ and plan to **continue to take actions** additional steps to remediate this material weakness, including (i) **designing and** implementing and documenting new processes and controls to help ensure the completeness and accuracy of our inventory reconciliations, (ii) engaging ~~additional third party subject matter experts and~~ accounting personnel with U. S. GAAP experience specific to inventory accounting, ~~and~~ (iii) enhancing the ~~accuracy of key reports used to calculate the firm purchase commitment and~~ (iv) **establishing effective** monitoring and oversight controls to help to ensure the completeness and accuracy of inventory included in our financial statements and related disclosures. However, we cannot provide assurance that we will be able to correct this material weakness in a timely manner or that our remediation efforts will be adequate to allow us to conclude that our internal control over financial reporting will be effective in the future. Even if this material weakness is remediated in the future, we could identify additional material weaknesses or deficiencies in our internal control over financial reporting that could require correction or **Akebia Therapeutics, Inc. | Form 10- K | Page 97** remediation. For example, we previously identified a material weakness in our internal control over financial reporting as of December 31, 2022 relating to our product return reserves that resulted in a revision of our financial statements for the years ended December 31, 2022, 2021 and 2020. In addition, our conclusion that we have a material weakness could give rise to increased scrutiny, review, audit and investigation over our accounting controls and procedures, which could then lead to additional areas of deficiency or errors in our financial statements. We will need to continue to dedicate internal resources, engage outside consultants and maintain a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to remediate the material weakness relating to our accounting for inventory and inventory related transactions described above and any future control deficiencies or material weaknesses, and improve control processes as appropriate, validate through testing that controls are functioning as documented and maintain a continuous reporting and improvement process for internal control over financial reporting. If we are not able to correct material weaknesses or deficiencies in internal controls in a timely manner or otherwise comply with the requirements of Section 404 in a timely manner, our ability to record, process, summarize and report financial information accurately and within applicable time periods may be adversely affected, and we could be subject to sanctions or investigations by the **Securities Exchange Commission, or the** SEC, the Nasdaq Stock Market or other regulatory authorities as well as stockholder litigation which, even if resolved in our favor, would require additional financial and management resources and could adversely affect the market price of our common stock. Any failure to maintain or implement required effective internal control over financial reporting, or any difficulties we encounter in their implementation, could result in additional material weaknesses, cause us to fail to meet our reporting obligations or result in material misstatements in our financial statements. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock and 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. **Akebia Therapeutics, Inc. | Form 10- K | Page 97** 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 and artificial intelligence based software, 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 and Vafseo. Additionally, the use of artificial intelligence based software is increasingly being used in the biopharmaceutical industry. Use of artificial intelligence based software may lead to the release of confidential proprietary information, which may impact our ability to realize the benefit of our intellectual property. 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. Attackers have used artificial intelligence and machine learning to launch more automated, targeted and coordinated attacks against targets. 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 U. S. 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, social engineering, zero day vulnerabilities or other unauthorized access or other significant compromise of our computer, communications and related systems. Although **Akebia Therapeutics, Inc. | Form 10- K | Page 98** 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 breaks, 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. Because the techniques used to obtain unauthorized access, disable or degrade service, or sabotage systems change frequently and continuously become more sophisticated, including the use of artificial intelligence to generate sophisticated spoofed emails and deep fake voice and video, 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; ~~**Akebia Therapeutics, Inc. | Form 10- K | Page 98**~~ 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 **Akebia Therapeutics, Inc. | Form 10- K | Page 99** • 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 MHRA and

TGA, and we conducted our global clinical trials for vadadustat **Vafseo**, 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 **Akebia Therapeutics, Inc. | Form 10-K | Page 99** 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 long-lived assets, including goodwill **and an intangible asset** as a result of the Merger. **The intangible Other long-lived asset assets has become impaired, including property and equipment, right-of-use assets or goodwill,** could become further impaired in the future under certain conditions. **Akebia Therapeutics, Inc. | Form 10** addition, other long-lived assets, including property and equipment, right- **K | Page 100** of-use assets or goodwill could become impaired in the future under certain conditions. Any potential future impairment of property and equipment, our right-of-use assets, **or goodwill or intangible asset** may significantly impact our results of operations and financial condition. As of December 31, **2023-2024**, we had approximately \$ **95.59. 1.0** million in the aggregate of goodwill **and a definite lived intangible asset** from the Merger, \$ **32.62** million of property and equipment and \$ **128.42** million right-of-use assets. In accordance with ASC 350, Goodwill and Other, we are required annually for goodwill, or more frequently upon certain indicators of impairment, to review our estimates and assumptions underlying the fair value of our goodwill **and intangible asset**. In addition, under ASC 360, Property, Plant and Equipment, we are required to review our property and equipment and right-of-use assets whenever events or changes in circumstances indicate that the carrying amount of an asset **or asset group** may not be recoverable. Events giving rise to impairment of long-lived 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 **and Vafseo'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 our

long-lived 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. The estimates, judgments and assumptions used in our impairment analyses, and the results of our analyses, are discussed in Note 2, Summary of Significant Accounting Policies, to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Form 10-K. 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 plant and equipment, right-of-use assets, ~~or 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 ~~Vafseo vadadustat, if approved~~. We face an inherent risk of product liability as a result of the clinical and commercial use of Auryxia and ~~vadadustat~~ **Vafseo and our product candidates**. For example, we may be sued if Auryxia, **Vafseo or our vadadustat product candidates** allegedly causes injury or is found to be otherwise unsuitable during clinical ~~Akebia Therapeutics, Inc. | Form 10-K | Page 100~~ 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~~ **Vafseo or affect the development of our product candidates**. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, product liability claims may result in: • decreased demand for Auryxia or ~~Vafseo 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, **Vafseo or our vadadustat product candidates**; • 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; • loss of revenue; • the inability to commercialize Auryxia or ~~Vafseo 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 **Akebia Therapeutics, Inc. | Form 10-K | Page 101** 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, auditing, **directors and officers insurance** 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. ~~Akebia Therapeutics, Inc. | Form 10-K | Page 101~~ 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 Second Amended and Restated Bylaws, 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 **Akebia Therapeutics, Inc. | Form 10-K | Page 102** 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 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 ~~Securities Exchange Act of 1934, as amended, or the Exchange Act, or the rules and regulations thereunder.~~ Any person or entity purchasing or otherwise acquiring any ~~Akebia Therapeutics, Inc. | Form 10-K | Page 102~~ 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 I, Item 3. Legal Proceedings in this Form 10-K, 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 Form 10-K 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 was held on March 13, 2024. At the conclusion of the hearing, the Court granted our motion to dismiss. 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 **and could result in substantial costs and divert management's attention**. 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, such as rising inflation and increasing interest rates. 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 \$ **1-2. 84 24** on **August 1-March 27, 2023-2024** and a low price of \$ **0. 51-86** on **April 5-June 25, 2023-2024** in the twelve- month period ending on December 31, **2023-2024**. During that time, the price of our common stock ranged from an intra- day low of \$ **0. 49-80** per share to an intra- day high of \$ **1-2. 84-48** 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, Vafseo vadadustat in Europe and, if and as approved in the U. S. and other 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 **Vafseo**, regulatory or legal developments in the U. S. 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 actions and, shareholder derivative lawsuits and other litigation**. See Part I, Item 3. Legal legal Proceedings **proceedings are often brought against companies for any of the risks described in this Form 10- K following a decline for- or information concerning volatility in the market price of their securities class action initiated against Keryx and certain current and former directors and officers of ours and Keryx's. We** In addition, we could be the target of **other such litigation or other legal proceedings** in the future. Class action **actions and, shareholder derivative lawsuits and other legal proceedings**, whether successful or not, could result in substantial costs, damage or settlement awards and **a diversion of such costs and any related settlements our- or judgments may not be covered by insurance** management's resources and attention from running our business, which could materially harm our reputation, financial condition and results of operations. Monetary Akebia Therapeutics, Inc. | Form 10- K | Page 103 common stock and our ability to access the capital markets could be negatively impacted. We must satisfy Nasdaq's continued listing requirements, including, among other things, a minimum closing bid price of \$ 1.00 per share and timely filing of all periodic financial reports, or risk delisting, which would have a material adverse effect on our business. If we fail to maintain compliance with Nasdaq's continued listing requirements, it could affect our ability to raise capital on acceptable terms, or at all. In the event we are delisted from Nasdaq, the only established trading market for our common stock would be eliminated, and we would be forced to list our shares on the OTC Markets or another quotation. 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 December 31, **2023-2024** and based on the amounts reported in the most recent filings **- filing made by BlackRock** under Section 13 (**d**) and 13 (**g**) of the Exchange Act, **BlackRock Muncer A. Satter, or Satter**, beneficially owned approximately **8-6. 3-2** % of our outstanding shares of common stock **, the Vanguard Group, or Vanguard, beneficially owned approximately 4. 0** % **. By selling a large number of our outstanding shares of common stock, and BlackRock could cause the price of our common stock to decline. In addition, as of December 31, 2024,** CSL Vifor beneficially owned **7, 571, 429** approximately **4** % of our outstanding shares of common stock **. By selling a large number of shares of common stock, which 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. Further** In addition, we entered into a warrant agreement with Kreos Capital VII Aggregator SCSp, an affiliate of Kreos, or the Warrant Holder, pursuant to which (i) we issued a warrant to the Warrant Holder to purchase 3, 076, 923 shares of our common stock, at an exercise price per share of \$ 1. 30 (subject to standard adjustments for stock splits, stock dividends, rights offerings and pro rata distributions), or the Exercise Price, and (ii) **if we drawdown the Tranche C Loan, at that time we will issue issued** a warrant to the Warrant Holder to purchase 1, 153, 846 shares of our common stock, at an exercise price per share equal to the Exercise Price. Each warrant is exercisable for eight years from **the** date of issuance. If any or all of the warrants are exercised, our stockholders could realize dilution, and the value of their shares could decrease. We have a significant number of shares that are subject to outstanding options **and, restricted stock units and other securities convertible into our common stock**, 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 on Form S-3, which allows us to offer and sell up to \$ 250.0 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 \$ 75.0 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 ~~any 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. **Akebia Therapeutics, Inc. | Form 10-K | Page 104** Our executive officers, directors and principal stockholders maintain the ability to significantly influence all matters submitted to stockholders for approval. As of December 31, ~~2023~~ **2024**, 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; ~~Akebia Therapeutics, Inc. | Form 10-K | Page 104~~ • 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 BlackRock Credit Agreement preclude us from paying cash dividends without prior written consent of the lender 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.