

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2023

OR

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

For the transition period from _____ to _____
Commission File No. 001-38944

Akero Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

81-5266573
(I.R.S. Employer
Identification No.)

601 Gateway Boulevard, Suite 350
South San Francisco, CA 94080
(650) 487-6488

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.0001 per share	AKRO	The Nasdaq Global Select Market

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

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

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

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

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

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

As of November 3, 2023, the registrant had 55,709,783 shares of common stock, \$0.0001 par value per share, outstanding.

SUMMARY OF THE MATERIAL RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous risks and uncertainties, including those described in Part II, Item 1A. “Risk Factors” in this Quarterly Report on Form 10-Q. The principal risks and uncertainties affecting our business includes:

- Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control, including difficulties in identifying patients with metabolic dysfunction-associated steatohepatitis (“NASH/MASH”), significant competition for recruiting such patients in clinical trials, and restrictions on patients and investigators related to outbreaks of infectious diseases or public health crises.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than us.
- Failures or delays in the commencement or completion of, or ambiguous or negative results from our planned clinical trials of our product candidates, could result in increased costs to us and could delay, prevent, or limit our ability to generate revenue and continue our business.
- Clinical development is uncertain and our clinical trials for efruxifermin (“EFX”) and any future product candidates may experience delays, which would adversely affect our ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.
- We rely and will continue to rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates.
- The manufacture of our product candidates is complex and we may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.
- We are heavily dependent on the success of EFX, our only product candidate.
- If we fail to develop and successfully commercialize other product candidates, our business and future prospects may be harmed and our business will be more vulnerable to any problems that we encounter in developing and commercializing our product candidate.
- We may develop EFX, and potentially future product candidates, in combination with other therapies, which exposes us to additional risks.
- If we are not successful in discovering, developing, receiving regulatory approval for and commercializing EFX and any future product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.
- We may be required to make significant payments under our license agreement for EFX.
- The regulatory approval processes of the U.S. Food and Drug Administration (the “FDA”) and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. Our inability to obtain regulatory approval for EFX or any future product candidate would substantially harm our business.
- Even if we are able to obtain regulatory approvals for our product candidate or any future product candidates, if they exhibit harmful side effects after approval, our regulatory approvals could be revoked or otherwise negatively impacted, and we could be subject to costly and damaging product liability claims.

- Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations, which, if violated, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.
- We have incurred significant losses since our inception and we expect to incur losses for the foreseeable future.
- We currently have a limited operating history, have not generated any revenue to date, and may never become profitable.
- We will require additional capital to finance our operations, which may not be available to us on acceptable terms, or at all. As a result, we may not complete the development and commercialization of our product candidate or develop any future product candidates.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). These statements involve risks, uncertainties, and other factors that may cause actual results, levels of activity, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements. All statements, other than statements of historical facts, contained in this Quarterly Report on Form 10-Q, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements include, among other things, statements about:

- the success, cost and timing of our product development activities and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs;
- our ability to successfully conduct and complete enrollment in two parallel, randomized, placebo-controlled clinical trials of our SYNCHRONY Phase 3 program for patients, our SYNCHRONY Histology and Real-World trials, subject to ongoing confirmation and feedback from FDA;
- our ability to successfully conduct and complete our ongoing 96-week Phase 2b clinical trial of EFX in patients with NASH/MASH who have F2 or F3 fibrosis, known as the HARMONY study, including the ability to obtain data and maintain our expected timelines;
- our ability to successfully conduct and complete our ongoing 96-week Phase 2b clinical trial of EFX in patients with NASH/MASH who have cirrhosis (F4 fibrosis, compensated), known as the SYMMETRY study, including the ability to obtain data and maintain our expected timelines;
- our ability to successfully expand the clinical trials for our SYNCHRONY Phase 3 program globally, including the enrollment of patients and activation of the first clinical trial sites in Israel and Turkey amidst the ongoing armed conflict in Israel and the Gaza Strip;
- our ability to reach agreement with FDA on the design of the third clinical trial in our SYNCHRONY Phase 3 program, SYNCHRONY Outcomes, and our ability to enroll patients and complete this trial;
- the timing and outcome of any meetings with regulatory authorities;
- our ability to meet the requirements of regulatory authorities to initiate and complete the SYNCHRONY Phase 3 studies of EFX in a timely manner;
- the potential for another pandemic, epidemic or outbreak of an infectious disease, such as COVID-19, to disrupt our business plans, product development activities, ongoing clinical trials, including the timing and enrollment of patients, the health of our employees and the strength of our supply chain;
- our ability to advance any product candidate into or successfully complete any clinical trial;
- our ability to successfully manufacture our product candidates for future clinical trials or for commercial use, if approved;
- the potential for our identified research priorities to advance our technologies;
- our ability to obtain and maintain regulatory approval, if obtained, of EFX or any future product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate;
- the ability to license additional intellectual property relating to any future product candidates and to comply with our existing license agreement;
- our ability to commercialize our products in light of the intellectual property rights of others;
- the success of competing therapies that are or become available;
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates;
- the commercialization of our product candidates, if approved;
- our plans to research, develop and commercialize our product candidates;
- our ability to attract collaborators with development, regulatory and commercialization expertise;

- future agreements with third parties in connection with the commercialization of our product candidates and any other approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates, if approved;
- regulatory developments in the United States and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the impact of laws and regulations; and
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Quarterly Report on Form 10-Q, particularly in the “Risk Factors” section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or into which we may enter.

You should read this Quarterly Report on Form 10-Q and the documents that we reference herein and have filed or incorporated by reference as exhibits hereto completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

NOTE REGARDING TRADEMARKS

Akero Therapeutics, Inc. is the owner of the AKERO trademark, as well as certain other trademarks, including design versions of some of these trademarks. The symbols TM and ® are not used in connection with the presentation of these trademarks in this report and their absence does not indicate a lack of trademark rights. Certain other trademarks used in this report are the property of third-party trademark owners and may be presented with or without trademark references.

All brand names or trademarks appearing in this report are the property of their respective owners. Unless the context requires otherwise, references in this report to “Akero,” the “Company,” “we,” “us” and “our” refer to Akero Therapeutics, Inc. and its subsidiary.

PART I—FINANCIAL INFORMATION**Item 1. Condensed Consolidated Financial Statements****Akero Therapeutics, Inc.**

Condensed Consolidated Balance Sheets
(In thousands, except share and per share amounts)
(Unaudited)

	September 30, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	\$ 269,546	\$ 249,773
Short-term marketable securities	285,186	101,676
Prepaid expenses and other current assets	21,247	3,724
Total current assets	575,979	355,173
Long-term marketable securities	58,264	—
Property and equipment, net	20	47
Right of use asset	1,068	1,242
Other assets, noncurrent	—	108
Total assets	<u>\$ 635,331</u>	<u>\$ 356,570</u>
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 11,454	\$ 7,968
Accrued expenses and other current liabilities	14,917	11,115
Loan payable, current	2,076	—
Total current liabilities	28,447	19,083
Loan payable, noncurrent	22,768	9,541
Warrant liability	93	305
Operating lease liability, noncurrent	888	1,079
Total liabilities	52,196	30,008
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Common stock, \$0.0001 par value, 150,000,000 shares authorized as of September 30, 2023 and December 31, 2022; 55,681,026 and 46,865,206 shares issued and outstanding as of September 30, 2023 and December 31, 2022, respectively	6	5
Additional paid-in capital	1,102,545	748,857
Accumulated other comprehensive (loss) income	(506)	37
Accumulated deficit	(518,910)	(422,337)
Total stockholders' equity	583,135	326,562
Total liabilities and stockholders' equity	<u>\$ 635,331</u>	<u>\$ 356,570</u>

The accompanying notes are an integral part of these condensed consolidated financial statements.

Akero Therapeutics, Inc.**Condensed Consolidated Statements of Operations and Comprehensive Loss**
(In thousands, except share and per share amounts)
(Unaudited)

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2023</u>	<u>2022</u>	<u>2023</u>	<u>2022</u>
Operating expenses:				
Research and development	\$ 38,634	\$ 25,087	\$ 88,406	\$ 66,964
General and administrative	7,981	11,004	22,591	22,772
Total operating expenses	46,615	36,091	110,997	89,736
Loss from operations	(46,615)	(36,091)	(110,997)	(89,736)
Interest expense	(888)	(324)	(2,202)	(377)
Other income, net	7,844	873	16,626	1,139
Net loss	(39,659)	(35,542)	(96,573)	(88,974)
Net unrealized (loss) gain on marketable securities	(255)	3	(543)	27
Comprehensive loss	\$ (39,914)	\$ (35,539)	\$ (97,116)	\$ (88,947)
Net loss per common share, basic and diluted	\$ (0.71)	\$ (0.92)	\$ (1.87)	\$ (2.45)
Weighted-average number of shares used in computing net loss per common share, basic and diluted	55,613,120	38,663,469	51,506,766	36,364,284

The accompanying notes are an integral part of these condensed consolidated financial statements.

Akero Therapeutics, Inc.
Condensed Consolidated Statements of Stockholders' Equity (Deficit)
(In thousands, except share amounts)
(Unaudited)

	Common Stock		Additional Paid-In- Capital	Accumulated Other Comprehensive Gain (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balances at December 31, 2022	46,865,206	\$ 5	\$ 748,857	\$ 37	\$ (422,337)	\$ 326,562
Exercise of stock options	105,783	—	456	—	—	456
Common stock issued for vested restricted stock units	8,067	—	—	—	—	—
Vested warrants issued pursuant to loan agreement	—	—	330	—	—	330
Stock-based compensation expense	—	—	4,844	—	—	4,844
Net unrealized loss on marketable securities	—	—	—	(16)	—	(16)
Net loss	—	—	—	—	(25,831)	(25,831)
Balances at March 31, 2023	46,979,056	\$ 5	\$ 754,487	\$ 21	\$ (448,168)	\$ 306,345
Exercise of stock options	306,510	—	1,556	—	—	1,556
Common stock issued for vested restricted stock units	9,956	—	—	—	—	—
Issuance of common stock pursuant to ESPP purchases	7,885	—	313	—	—	313
Issuance of common stock pursuant to At-The-Market ("ATM") offering, net of issuance costs	3,006,052	—	123,824	—	—	123,824
Issuance of common stock pursuant to a direct offering, net of issuance costs	5,238,500	1	210,955	—	—	210,956
Stock-based compensation expense	—	—	4,798	—	—	4,798
Net unrealized loss on marketable securities	—	—	—	(272)	—	(272)
Net loss	—	—	—	—	(31,083)	(31,083)
Balances at June 30, 2023	55,547,959	\$ 6	\$ 1,095,933	\$ (251)	\$ (479,251)	\$ 616,437
Exercise of stock options	123,094	—	873	—	—	873
Common stock issued for vested restricted stock units	9,973	—	—	—	—	—
Stock-based compensation expense	—	—	5,739	—	—	5,739
Net unrealized loss on marketable securities	—	—	—	(255)	—	(255)
Net loss	—	—	—	—	(39,659)	(39,659)
Balances at September 30, 2023	55,681,026	\$ 6	\$ 1,102,545	\$ (506)	\$ (518,910)	\$ 583,135
Balances at December 31, 2021	34,900,727	\$ 4	\$ 479,436	\$ (27)	\$ (310,304)	\$ 169,109
Exercise of stock options	122,208	—	147	—	—	147
Stock-based compensation expense	—	—	3,311	—	—	3,311
Net unrealized loss on marketable securities	—	—	—	(3)	—	(3)
Net loss	—	—	—	—	(26,029)	(26,029)
Balances at March 31, 2022	35,022,935	\$ 4	\$ 482,894	\$ (30)	\$ (336,333)	\$ 146,535
Issuance of common stock pursuant to ESPP purchases	22,139	—	178	—	—	178
Issuance of common stock pursuant to equity investment by Pfizer, net of issuance costs	2,525,252	—	24,647	—	—	24,647
Vested warrants issued pursuant to loan agreement	—	—	227	—	—	227
Stock-based compensation expense	—	—	4,161	—	—	4,161
Net unrealized gain on marketable securities	—	—	—	27	—	27
Net loss	—	—	—	—	(27,403)	(27,403)
Balances at June 30, 2022	37,570,326	\$ 4	\$ 512,107	\$ (3)	\$ (363,736)	\$ 148,372
Issuance of common stock upon closing of follow-on public offering, net of issuance costs	8,846,154	1	215,835	—	—	215,836
Exercise of stock options	240,998	—	3,108	—	—	3,108
Stock-based compensation expense	—	—	11,731	—	—	11,731
Net unrealized gain on marketable securities	—	—	—	3	—	3
Net loss	—	—	—	—	(35,542)	(35,542)
Balances at September 30, 2022	46,657,478	\$ 5	\$ 742,781	\$ —	\$ (399,278)	\$ 343,508

The accompanying notes are an integral part of these condensed consolidated financial statements.

Akero Therapeutics, Inc.
Condensed Consolidated Statements of Cash Flows
(In thousands)
(Unaudited)

	Nine Months Ended September 30,	
	2023	2022
CASH FLOWS FROM OPERATING ACTIVITIES		
Net loss	\$ (96,573)	\$ (88,974)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	15,381	19,203
Depreciation	27	33
Non-cash lease expense	174	162
Net amortization of premiums and discounts on short-term investments	(5,908)	182
Amortization of debt issuance costs and discount	328	110
Fair value change in warrant liability	118	29
Write-off of deferred offering costs	337	—
Unrealized foreign exchange gain and loss	(26)	(12)
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(17,793)	2,657
Accounts payable	3,584	(708)
Accrued expenses and other current liabilities	3,782	460
Operating lease liability	(171)	(151)
Net cash used in operating activities	<u>(96,740)</u>	<u>(67,009)</u>
CASH FLOWS FROM INVESTING ACTIVITIES		
Purchase of short-term and long-term marketable securities	(374,909)	—
Proceeds from maturities of short-term marketable securities	138,500	37,620
Net cash (used in) provided by investing activities	<u>(236,409)</u>	<u>37,620</u>
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from the exercise of stock options	2,817	2,229
Proceeds from the issuance of common stock pursuant to employee stock purchase plan purchases	313	178
Proceeds from the issuance of common in a follow-on public offering	—	216,200
Proceeds from the issuance of common stock pursuant to the ATM offering	124,212	—
Proceeds from the issuance of common stock pursuant to registered direct offering	211,217	—
Proceeds from the issuance of common stock pursuant to private offering	—	25,000
Proceeds from loan payable	15,000	10,000
Payment of debt and equity issuance costs	(745)	(698)
Net cash provided by financing activities	<u>352,814</u>	<u>252,909</u>
Net increase in cash, cash equivalents and restricted cash	19,665	223,520
Cash, cash equivalents and restricted cash at the beginning of the period	249,881	150,591
Cash, cash equivalents and restricted cash at the end of the period	<u>\$ 269,546</u>	<u>\$ 374,111</u>
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Cash paid for interest	\$ 1,715	\$ 189
NON-CASH INVESTING AND FINANCING INFORMATION:		
Change in net unrealizable (loss) gain on marketable securities	\$ (543)	\$ 27
Warrant liability costs reclassified to additional paid-in equity on vested warrants issued	\$ 330	\$ —
Debt and equity issuance costs included in accounts payable and accrued expenses and other current liabilities	\$ —	\$ 371
Deferred offering costs reclassified to additional paid-in equity	\$ 364	\$ 150
Stock options exercises included in other current assets	\$ 67	\$ —

The accompanying notes are an integral part of these condensed consolidated financial statements.

Akero Therapeutics, Inc.**Notes to Unaudited Condensed Consolidated Financial Statements**
(Amounts in thousands, except share and per share data)**1. Nature of the business and basis of presentation**

Akero Therapeutics, Inc., together with its wholly owned subsidiary Akero Securities Corporation, (“Akero” or the “Company”) is a clinical-stage company dedicated to developing transformational treatments for patients with serious metabolic diseases marked by high unmet medical need, including metabolic dysfunction-associated steatohepatitis (“NASH/MASH”) a disease without any approved therapies. NASH/MASH is a severe form of metabolic dysfunction-associated steatotic liver disease (“MASLD”) characterized by inflammation and fibrosis in the liver that can progress to cirrhosis, liver failure, cancer and death. The Company’s lead product candidate is efruxifermin (“EFX”), an analog of fibroblast growth factor 21 (“FGF21”) which is an endogenously expressed hormone that protects against cellular stress and regulates metabolism of lipids, carbohydrates and proteins throughout the body. The Company has initiated a Phase 3 program called SYNCHRONY, for which the first two of three planned clinical trials evaluating EFX have begun screening. EFX is also being evaluated in two ongoing, 96-week Phase 2b clinical trials in patients with biopsy-confirmed NASH/MASH: the HARMONY study in patients with pre-cirrhotic NASH/MASH (F2-F3 fibrosis) and the SYMMETRY study in patients with cirrhotic NASH/MASH (F4 fibrosis, compensated). In the third quarter of 2022, the Company reported Week 24 results from the 96-Week HARMONY study, which showed statistically significant response rates for both the 50mg and 28mg dose groups on both fibrosis regression and NASH resolution among patients with biopsy-confirmed NASH/MASH. In October 2023, the Company reported Week 36 results of the 96-week Phase 2b SYMMETRY study in biopsy-confirmed NASH/MASH patients with compensated cirrhosis (F4, Child-Pugh class A), which showed a trend of 22% and 24% of patients in the 28mg and 50mg EFX-treated groups, respectively, experiencing at least a one-stage improvement in liver fibrosis and no worsening of NASH, compared with 14% for placebo and statistically significant response rates for NASH resolution observed in 67% and 60% of patents in the 28mg and 50mg EFX-treated groups, respectively, compared with 26% for placebo. Based on these and other data, the Company believes EFX has the potential, if approved, to be an important medicine for treating NASH/MASH.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, completion and success of clinical testing, development by competitors of new technological innovations, compliance with governmental regulations, dependence on key personnel and protection of proprietary technology and the ability to secure additional capital to fund operations. EFX will require extensive clinical testing prior to regulatory approval and commercialization. These efforts require significant amounts of additional capital, adequate personnel, and infrastructure and extensive compliance-reporting capabilities. Even if the Company’s drug development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Basis of presentation

The accompanying condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (“GAAP”) and include the accounts of the Company after elimination of all intercompany accounts and transactions. All adjustments necessary for the fair presentation of the Company’s condensed consolidated financial statements for the periods presented have been reflected.

Liquidity

In accordance with Accounting Standards Update (“ASU”) No. 2014-15, *Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are certain conditions and events, considered in the aggregate, that raise substantial doubt about the Company’s ability to continue as a going concern within one year after the date that the condensed consolidated financial statements are issued.

Akero Therapeutics, Inc.**Notes to Unaudited Condensed Consolidated Financial Statements**
(Amounts in thousands, except share and per share data)

Since its inception, the Company has funded its operations primarily with \$90,500 in proceeds from the sale of redeemable convertible preferred stock, \$105,800 in proceeds from its initial public offering (“IPO”) in June 2019, and \$818,900 in proceeds from the sales of common stock in equity offerings, including a \$25,000 equity investment from Pfizer, Inc., in 2020, 2022 and 2023. The Company has incurred recurring losses since its inception, including net losses of \$96,573 and \$88,974 for the nine months ended September 30, 2023 and 2022, respectively, and net losses of \$112,033 and \$100,777 for the years ended December 31, 2022 and 2021, respectively. In addition, as of September 30, 2023, the Company had an accumulated deficit of \$518,910. The Company expects to continue to generate operating losses for the foreseeable future. As of November 13, 2023, the issuance date of these condensed consolidated financial statements, the Company expects that its existing cash, cash equivalents, short-term and long-term marketable securities of \$612,996 as of September 30, 2023, will be sufficient to fund its operating expenses and capital expenditure requirements for at least 12 months from the issuance date of these condensed consolidated financial statements. The Company expects that it will require additional funding to complete the clinical development of EFX, commercialize EFX, if it receives regulatory approval, and pursue in-licenses or acquisitions of other product candidates.

If the Company is unable to obtain funding, the Company will be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations. Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

2. Summary of significant accounting policies***Unaudited interim financial statements***

The accompanying unaudited condensed consolidated financial statements have been prepared by the Company in accordance with GAAP for interim financial reporting and as required by Regulation S-X, Rule 10-01. The unaudited condensed consolidated financial statements have been prepared on the same basis as the Company’s audited annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for a fair statement of the Company’s condensed consolidated balance sheet as of September 30, 2023, the condensed consolidated statements of operations and comprehensive loss for the three and nine months ended September 30, 2023 and 2022, the condensed consolidated statement of stockholders’ equity (deficit) as of September 30, 2023 and the condensed consolidated statements of cash flows for the nine months ended September 30, 2023. The financial data and other information disclosed in these notes related to the three and nine months ended September 30, 2023 and 2022 are unaudited. The results for the three and nine months ended September 30, 2023 are not necessarily indicative of results to be expected for the year ending December 31, 2023, any other interim periods, or any future year or period.

Use of estimates

The preparation of the Company’s condensed consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the condensed consolidated financial statements, and the reported amounts of expenses during the reporting period. Significant estimates and assumptions reflected in these condensed consolidated financial statements include, but are not limited to, the recognition of research and development expenses, stock-based compensation expense, warrant liabilities and the valuation allowance for deferred tax assets. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates when there are changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates.

Akero Therapeutics, Inc.**Notes to Unaudited Condensed Consolidated Financial Statements**
(Amounts in thousands, except share and per share data)***Cash and cash equivalents***

The Company considers all highly liquid investments with original maturities of three months or less at the time of purchase to be cash equivalents. Cash equivalents consist primarily of amounts invested in money market accounts.

Short-term and long-term marketable securities

The Company invests in short and long-term marketable securities, primarily money market funds, commercial paper, U.S. treasury securities and corporate debt securities. The Company continually evaluates the credit ratings of its investment portfolio and underlying securities. The Company invests in accordance with its investment policy and invests at the date of purchase in securities with high ratings from top rating agencies. The Company classifies its short-term and long-term marketable securities as available-for-sale securities and reports them at fair value in short-term and long-term marketable securities on the condensed consolidated balance sheets with related unrealized gains and losses included within accumulated other comprehensive gain (loss) on the condensed consolidated balance sheets. The amortized cost of marketable securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in other income on the condensed consolidated statements of operations and comprehensive loss. When the fair value is below the amortized cost of a marketable security, the Company reviews and determines whether the impairment is due to credit-related factors or noncredit-related factors. The credit-related impairment amount is recognized in other income on the condensed consolidated statements of operations and comprehensive loss, with a corresponding allowance for credit losses account in the condensed consolidated balance sheet. Subsequent improvements in expected credit losses are recognized as a reversal of an amount in the allowance account. If the Company has the intent to sell the security or it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis, then the allowance for the credit loss is written-off and the excess of the amortized cost basis of the asset over its fair value is recorded in the condensed consolidated statements of operations. There were no credit losses recorded during the periods ended September 30, 2023 and December 31, 2022.

Restricted cash

As of December 31, 2022, the Company was required to maintain a separate cash balance of \$108 for the benefit of the landlord in connection with the Company's Gateway office space lease in South San Francisco, California (the "Gateway Lease"), which is classified within other assets (non-current) on the condensed consolidated balance sheets (see Note 12). The Company was not required to maintain a separate cash balance for the benefit of the landlord as of September 30, 2023.

Concentrations of credit risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash, cash equivalents, short and long-term marketable securities. Periodically, the Company maintains deposits in accredited financial institutions in excess of federally insured limits. The Company deposits its cash investments in financial institutions that it believes have high credit quality and has not experienced any losses on such accounts and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships. At September 30, 2023, all of the Company's cash, cash equivalents, short and long-term investments were held at four accredited financial institutions.

Akero Therapeutics, Inc.**Notes to Unaudited Condensed Consolidated Financial Statements**
(Amounts in thousands, except share and per share data)

As of December 31, 2022, the Company held cash deposits at Silicon Valley Bank ("SVB") in excess of government insured limits. On March 10, 2023, SVB was closed by the California Department of Financial Protection and Innovation, and the Federal Deposit Insurance Corporation ("FDIC") was appointed as receiver. No losses were incurred by the Company on deposits that were held at SVB. Management believes that the Company is not currently exposed to significant credit risk as the vast majority of the Company's deposits were either owned directly by the Company and held in custody at a third-party financial institution or, subsequent to March 10, 2023, have been transferred to a third-party financial institution. On March 27, 2023, SVB was acquired by First-Citizen BancShares, Inc ("First-Citizen"). As of September 30, 2023, the Company did not have any significant deposits on account at or relationships with SVB or First-Citizen.

Leases

The Company determines whether an arrangement is or contains a lease at inception by assessing whether the arrangement contains an identified asset and whether the Company has the right to control the identified asset. Right-of-use ("ROU") assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Lease liabilities are recognized at the lease commencement date based on the present value of future lease payments over the lease term. ROU assets are based on the measurement of the lease liability and are further adjusted by any lease payments made prior to or on lease commencement, lease incentives received and initial direct costs incurred, as applicable. The Company has elected not to recognize leases with a lease term of one year or less on its balance sheet. Operating lease costs included in the measurement of the lease are recognized on a straight-line basis over the lease term. Variable lease costs are expensed as incurred as an operating expense.

The Company determines the lease classification and the present value of future lease payments at the time of the lease commencement using an incremental borrowing rate that it estimates based upon the Company's credit risk and term of the lease. The interest rate implicit in lease contracts has not historically been readily determinable and the Company must therefore use the appropriate incremental borrowing rate to measure its leases. To estimate the incremental borrowing rate, a credit rating applicable to the Company is estimated using a synthetic credit rating analysis since the Company does not currently have a rating agency-based credit rating.

Research and development costs

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred to discover, research and develop drug candidates, including personnel expenses, stock-based compensation expense, third-party license fees and external costs including fees paid to consultants, contract manufacturing organizations ("CMOs") and clinical research organizations ("CROs") in connection with drug product manufacturing, nonclinical studies and clinical trials, and other related clinical trial fees, such as for investigator grants, patient screening, laboratory work, clinical trial database management, clinical trial material management and statistical compilation and analysis. Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

Foreign currency transaction gains and losses related to the purchase of contract manufacturing services are included as a component of research and development expense.

Costs incurred in obtaining technology licenses are charged immediately to research and development expense if the technology licensed has not reached technological feasibility and has no alternative future uses.

Akero Therapeutics, Inc.**Notes to Unaudited Condensed Consolidated Financial Statements**
(Amounts in thousands, except share and per share data)***Research contract costs and accruals***

The Company has entered into various research and development and other agreements with commercial firms, researchers and others for provisions of goods and services. These agreements are generally cancelable, and the related costs are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research and development costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies or clinical trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ materially from the Company's estimates.

Stock-based compensation

The Company grants stock-based awards from its stock compensation plans (see Note 8). The Company measures all stock-based awards granted to employees and nonemployees based on the fair value on the date of the grant and recognizes compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award, on a straight-line basis. The Company recognizes stock-based compensation expense for awards that contain performance-based conditions using the accelerated attribution method when management determines it is probable that the performance condition will be satisfied. The Company accounts for forfeitures as they occur. Stock-based compensation for restricted stock units is measured based on the market closing price of our common stock on the grant date. Stock-based compensation expense is recognized on a straight-line basis over the requisite service period, generally four years.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option, and the Company's expected dividend yield. The Company went public in June 2019 and accordingly, lacks sufficient company-specific historical and implied volatility information for its shares traded in the public markets. Therefore, it estimates its expected share price volatility based on the historical volatility of publicly traded peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded share price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future. The fair value of each common stock award is estimated on the date of grant based on the fair value of the Company's common stock on that same date.

Compensation expense for purchases under the Employee Stock Purchase Plan is recognized based on the fair value of the common stock estimated based on the closing price of our common stock as reported on the date of offering, less the purchase discount percentage provided for in the plan.

The Company classifies stock-based compensation expense in its condensed consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Loan Payable

Loan Payable represents the Loan and Security Agreement, dated June 15, 2022 ("Loan Agreement") with Hercules Capital, Inc. ("Hercules"), which the Company has accounted for as a debt financing arrangement. Interest expense is accrued using the effective interest rate method over the estimated period the loan will be repaid. Loan issuance costs have been recorded as a debt discount in the condensed consolidated balance sheets and are being

Akero Therapeutics, Inc.**Notes to Unaudited Condensed Consolidated Financial Statements**
(Amounts in thousands, except share and per share data)

amortized and recorded as interest expense throughout the life of the Loan Agreement using the effective interest rate method. The Company determined that there are not any embedded features in the Loan Agreement that require bifurcation and separate accounting as derivative financial instruments pursuant to Accounting Standards Codification ("ASC") Topic 815, *Derivatives and Hedging*.

Warrant Liabilities

The Company accounts for warrants anticipated to be issued in the future under the Loan Agreement as liabilities and measures them at fair value using the Black-Scholes valuation model. The warrants are subject to remeasurement at each prospective balance sheet date, with any changes in the fair value recorded in the condensed consolidated statements of operations.

Comprehensive loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. The Company's comprehensive loss is comprised of net loss and changes in unrealized gains and losses on its short and long-term marketable securities.

Recently adopted accounting pronouncements

As of September 30, 2023, and for the period then ended, there were no recently adopted accounting standards that had a material impact on the Company's condensed consolidated financial statements. There were no recently issued accounting standards not yet adopted which would have a material effect on the Company's condensed consolidated financial statements.

3. Fair value measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

Akero Therapeutics, Inc.
Notes to Unaudited Condensed Consolidated Financial Statements
(Amounts in thousands, except share and per share data)

The following is a summary of our financial assets and liabilities measured at fair value on a recurring basis as of September 30, 2023 and December 31, 2022:

	September 30, 2023			
	Total	Level 1	Level 2	Level 3
Money market funds	\$ 261,202	\$ 261,202	\$ —	\$ —
U.S. Treasury securities	96,766	96,766	—	—
U.S. Government agency securities	144,418	—	144,418	—
Commercial paper	86,678	—	86,678	—
Corporate debt securities	15,589	—	15,589	—
Total assets	<u>\$ 604,653</u>	<u>\$ 357,968</u>	<u>\$ 246,685</u>	<u>\$ —</u>
Warrant liabilities	\$ 93	\$ —	\$ —	\$ 93
Total liabilities	<u>\$ 93</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 93</u>

	December 31, 2022			
	Total	Level 1	Level 2	Level 3
Money market funds	\$ 137,286	\$ 137,286	\$ —	\$ —
U.S. Treasury securities	58,721	58,721	—	—
Corporate debt securities	5,476	—	5,476	—
U.S. Government agency securities	62,955	—	62,955	—
Commercial paper	27,738	—	27,738	—
Total assets	<u>\$ 292,176</u>	<u>\$ 196,007</u>	<u>\$ 96,169</u>	<u>\$ —</u>
Warrant liabilities	\$ 305	\$ —	\$ —	\$ 305
Total liabilities	<u>\$ 305</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 305</u>

Corporate debt, commercial paper and U.S. Government agency securities were valued by the Company using quoted prices in active markets for similar securities, which represent a Level 2 measurement within the fair value hierarchy.

The carrying values of the Company's prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to the short-term nature of these assets and liabilities. During the three and nine months ended September 30, 2023 and the twelve months ended December 31, 2022, there were no transfers between Level 1, Level 2 and Level 3.

The Loan Payable is classified as a Level 3 liability. As of September 30, 2023, the carrying value of the Loan Payable approximates its fair value. The Company estimated the fair value of the warrant liabilities using the Black-Scholes model based on key assumption and inputs (see Note 6). The Company utilizes a probability assessment to estimate the likelihood of vesting for the remaining Loan Agreement warrants and allocated the probability of occurrence percentage to the fair values calculated.

Akero Therapeutics, Inc.
Notes to Unaudited Condensed Consolidated Financial Statements
(Amounts in thousands, except share and per share data)
4. Marketable securities

The following is a summary of marketable securities as of September 30, 2023 and December 31, 2022:

	September 30, 2023				
	Amortized cost	Gross unrealized gains	Gross unrealized losses	Credit losses	Fair value
Money market funds	\$ 261,202	\$ —	\$ —	\$ —	\$ 261,202
U.S. Treasury securities	96,945	—	(179)	—	96,766
U.S. Government agency securities	144,551	14	(147)	—	144,418
Commercial paper	86,852	—	(174)	—	86,678
Corporate debt securities	15,608	—	(19)	—	15,589
	<u>\$ 605,158</u>	<u>\$ 14</u>	<u>\$ (519)</u>	<u>\$ —</u>	<u>\$ 604,653</u>
Cash equivalents					\$ 261,202
Short-term marketable securities					285,186
Long-term marketable securities					58,264
					<u>\$ 604,652</u>
	December 31, 2022				
	Amortized cost	Gross unrealized gains	Gross unrealized losses	Credit losses	Fair value
Money market funds	\$ 137,286	\$ —	\$ —	\$ —	\$ 137,286
U.S. Treasury securities	58,698	23	—	—	58,721
Corporate debt securities	5,478	—	(2)	—	5,476
U.S. Government agency securities	62,939	15	—	—	62,954
Commercial paper	27,739	—	—	—	27,739
	<u>\$ 292,140</u>	<u>\$ 38</u>	<u>\$ (2)</u>	<u>\$ —</u>	<u>\$ 292,176</u>
Cash equivalents					\$ 190,500
Short-term marketable securities					101,676
					<u>\$ 292,176</u>

The following table presents the contractual maturities of our short and long-term marketable securities as of September 30, 2023 and December 31, 2022.

	September 30, 2023	December 31, 2022
Due within one year	\$ 285,186	\$ 101,676
Due after one year through five years	58,264	—
Total	<u>\$ 343,450</u>	<u>\$ 101,676</u>

Akero Therapeutics, Inc.**Notes to Unaudited Condensed Consolidated Financial Statements**
(Amounts in thousands, except share and per share data)**5. Accrued expenses and other current liabilities**

The following is a summary of accrued expenses and other current liabilities as of September 30, 2023 and December 31, 2022:

	<u>September 30, 2023</u>	<u>December 31, 2022</u>
Accrued external research and development expenses	\$ 10,734	\$ 9,789
Accrued employee compensation and benefits	3,404	804
Accrued legal and professional fees	274	197
Short-term lease liability and other	505	325
	<u>\$ 14,917</u>	<u>\$ 11,115</u>

6. Loan Payable and Warrant Liability

On June 15, 2022, the Company entered into the Loan Agreement with Hercules for an aggregate principal amount of \$100,000 (“Term Loan”). Pursuant to the Loan Agreement, the Term Loan is available to the Company in four tranches, subject to certain terms and conditions.

Under the terms of the Loan Agreement, the Company received \$10,000 upon closing, \$15,000 was borrowed on March 10, 2023 and an additional \$10,000 is available to the Company at its sole discretion until December 15, 2023. An additional \$20,000 will become available to the Company upon the achievement of certain clinical and financial milestones. An additional \$45,000 may become available to the Company at Hercules' sole discretion.

The Term Loan will mature on January 1, 2027 (the “Maturity Date”). The Term Loan bears interest at a variable annual rate equal to the greater of (a) 7.65% and (b) the Prime Rate (as reported in the Wall Street Journal) plus 3.65% (the “Interest Rate”). The Company may make payments of interest only through July 1, 2024, which may be extended to July 1, 2025 upon the achievement of the third tranche milestones (the “interest-only period”). After the interest-only period, the principal balance and related interest will be required to be repaid in equal monthly installments and continuing until the Maturity Date.

The Loan Agreement contains customary closing fees, events of default, and representations, warranties and covenants, including a financial covenant requiring the Company to maintain a minimum cash balance in relation to the outstanding principal balance of the Term Loan. The Loan Agreement provides for a prepayment charge equal to 3% of the outstanding principal balance of the Term Loan if prepayment is made within the first twelve months after closing, 2% if within the second twelve months after closing and 1% thereafter. In addition, the Loan Agreement provides for an End of Term Charge that will be the greater of 5.85% of the outstanding principal balance or \$1,463, which is recognized as a debt discount and is being accreted into the amortization of debt issuance costs and discount using the effective interest rate method over the term of the loan payable.

Upon closing, the Company issued warrants to Hercules to purchase shares of the Company’s common stock, par value \$0.0001 per share (“common stock”). The amount of shares that may be purchased for the Warrants will not exceed 1.5% multiplied by the greater of Tranche I and the aggregate original amount of the term loan advances, divided by the exercise price of the Warrants.

The Company was in compliance with all covenants of the Loan Agreement as of September 30, 2023.

The Company determined in accordance with ASC 480-10 that the initial tranche one advance of \$10,000, the additional Term Loan advances available under tranches one, two, three and four and the warrants issued upon closing shall be accounted for as freestanding financial instruments as they are legally detachable and separately exercisable.

Akero Therapeutics, Inc.**Notes to Unaudited Condensed Consolidated Financial Statements**
(Amounts in thousands, except share and per share data)

The Company also determined in accordance with ASC 815-10 that the additional Term Loan advances available under tranches one, two, three and four do not qualify as derivative instruments and that the value associated with these commitments is immaterial.

Upon closing, the Company issued to Hercules warrants to purchase 36,718 shares of Company's common stock and recognized the initial warrants at their relative fair value of \$227 in shareholders equity. In accordance with ASC 815-40, the additional remaining warrants to purchase shares of the Company's common stock at the closing of the Loan Agreement were recognized at their fair value of \$41 as warrant liabilities given the variable settlement amount of the warrant shares. The additional remaining warrants under the Loan Agreement are considered an outstanding instrument at close of the Loan Agreement. The total fair value of \$268 associated with these equity and liability classified warrants, is recognized as a debt discount and is being accreted into the amortization of debt issuance costs and discount using the effective interest rate method over the term of the loan payable. The Company reassesses the fair value of the warrant liability at the end of each reporting period.

On March 10, 2023, the Company borrowed an additional \$15,000 and issued warrants to Hercules to purchase an additional 9,180 shares of Company's common stock. The fair value associated with these additional warrants of \$330 were reclassified from warrant liability to additional paid in capital.

The warrant liabilities were valued at \$93 as of September 30, 2023.

Future principal debt payments on the currently outstanding loan payable as of September 30, 2023 are as follows (in thousands):

2023 (remaining period)	\$	—
2024		4,225
2025		9,278
2026		10,488
2027		1,009
Total principal outstanding		25,000
End of term charge		1,463
Total principal outstanding and end of term charge		26,463
Unamortized discount and issuance costs		(1,619)
Loan Payable	\$	24,844
Loan Payable - current		2,076
Loan Payable - noncurrent		22,768
Loan Payable	\$	24,844

The Company estimated the fair value of the warrant liability as of September 30, 2023 using probability assumptions of achieving the future milestones and using the Black-Scholes model based on the following key assumptions:

	As of September 30, 2023
Expected term (in years)	5.7
Expected volatility	79.55 %
Risk-free interest rate	4.60 %
Expected dividend yield	0.00 %

Akero Therapeutics, Inc.**Notes to Unaudited Condensed Consolidated Financial Statements**
(Amounts in thousands, except share and per share data)**7. Stockholder's equity (deficit)*****Common stock***

As of September 30, 2023 and December 31, 2022, the Company's certificate of incorporation, as amended and restated, authorized the Company to issue 150,000,000 shares of \$0.0001 par value common stock. Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. The holders of common stock, voting exclusively and as a separate class, have the exclusive right to vote for the election of directors of the Company. Common stockholders are entitled to receive dividends, as may be declared by the board of directors. Through September 30, 2023, no cash dividends had been declared or paid.

On June 24, 2019, the Company completed its IPO at which time the Company issued 6,612,500 shares of common stock, including the exercise in full by the underwriters of their option to purchase up to 862,500 additional shares of common stock, at a public offering price of \$16.00 per share. The Company received \$98,394, net of underwriting discounts and commissions, but before deducting offering costs paid by the Company, which were \$2,942. Upon the closing of the IPO, all outstanding shares of convertible preferred stock converted into 21,056,136 shares of common stock.

On July 10, 2020, the Company completed a follow-on public offering at which time the Company issued 6,012,390 shares of common stock, including the exercise in full by the underwriters of their option to purchase up to 784,224 additional shares of common stock, at a public offering price of \$36.00 per share. The Company received \$203,460 net of underwriting discounts and commissions, but before deducting offering costs paid by the Company.

On May 18, 2021, the Company filed a Form S-3 Registration Statement and the accompanying prospectus activating an At-The-Market ("ATM"), facility by entering into a sales agreement with J.P. Morgan Securities LLC, relating to shares of the Company's common stock offered. Pursuant to the terms of the sales agreement, the Company may offer and sell shares of common stock, having an aggregate price of up to \$100,000, from time to time. The Company reserved 5,000,000 shares of common stock related to the ATM offering. In March 2023, the Company terminated the sales agreement with J.P. Morgan Securities LLC and separately entered into a sales agreement with Jefferies LLC (the "Sales Agreement"). Pursuant to the Sales Agreement, the Company filed a prospectus supplement on March 17, 2023, under which the Company may offer and sell shares of common stock, having an aggregate value of up to \$200,000. In April and May 2023, the Company sold 3,006,052 shares of common stock under the Sales Agreement, at an average price of \$42.38 per share. The Company received net proceeds of \$123,824, after deducting sales agent commissions and issuance costs incurred by the Company of approximately \$3,578.

On June 15, 2022, the Company entered into a securities purchase agreement for the sale of 2,525,252 shares of the Company's common stock to Pfizer Inc. at \$9.90 per share in a registered direct offering conducted without an underwriter or placement agent and pursuant to the Company's effective shelf registration statement on Form S-3ASR and a related prospectus supplement filed with the SEC. The offering closed on June 17, 2022 for net proceeds of \$24,647, after deducting offering costs paid by the Company.

On September 19, 2022, the Company completed a follow-on public offering at which time the Company issued 8,846,154 shares of common stock, including the exercise in full by the underwriters of their option to purchase up to 1,153,846 additional shares of common stock, at a public offering price of \$26.00 per share. The Company received \$216,200 net of underwriting discounts and commissions of \$13,800, but before deducting offering costs incurred by the Company.

On May 16, 2023, the Company entered into an underwriting agreement (the "Underwriting Agreement") with Jefferies LLC, ("Jefferies"), as a representative of the several underwriters, pursuant to which the Company agreed to issue and sell 5,238,500 shares of the Company's common stock at \$42.00 per share in a registered direct offering

Akero Therapeutics, Inc.**Notes to Unaudited Condensed Consolidated Financial Statements**
(Amounts in thousands, except share and per share data)

pursuant to the Company's effective shelf registration statement on Form S-3ASR and a related prospectus supplement filed with the SEC. The offering closed on May 16, 2023. The Company received net proceeds of \$210,956, after deducting underwriters commissions and offering costs incurred by the Company of approximately \$9,061.

As of September 30, 2023 and December 31, 2022, there were 55,681,026 and 46,865,206 shares of common stock issued and outstanding, respectively.

The following shares of common stock were reserved for issuance as follows:

	<u>September 30, 2023</u>	<u>December 31, 2022</u>
Options outstanding under the 2018 Stock Option and Grant Plan	1,171,581	1,633,173
Options outstanding under the 2019 Stock Option and Incentive Plan	4,579,020	4,146,831
Restricted stock units outstanding under the 2019 Stock Option and Incentive Plan	142,498	129,131
Warrants to purchase common stock associated with Loan Agreement	45,898	36,718
Options available for future grant	3,365,403	2,038,142
Warrants available for future grant	137,700	146,880
Common stock available for ATM program	2,708,234	5,000,000
2019 Employee Stock Purchase Plan	1,590,426	1,187,508
	<u>13,740,760</u>	<u>14,318,383</u>

Undesignated preferred stock

The Company's fourth amended and restated certificate of incorporation authorizes the Company to issue up to 10,000,000 shares of undesignated preferred stock, par value \$0.0001 per share. There were no undesignated preferred shares issued or outstanding as of September 30, 2023.

Warrants Associated with Loan Agreement

In connection with the entry into the Loan Agreement, the Company issued to Hercules warrants to purchase shares of the Company's common stock. The amount of shares that may be purchased for the Warrants will not exceed 1.5% multiplied by the greater of Tranche I and the aggregate original amount of the term loan advances, divided by the exercise price of the Warrants. Upon execution of the Loan Agreement on June 15, 2022, the Company issued 36,718 warrants to purchase shares of the Company's common stock and recorded the initial warrants at their relative fair value in shareholder's equity. In March 2023, the Company issued an additional 9,180 warrants to purchase shares of the Company's common stock to Hercules in connection with the borrowing on March 10, 2023.

8. Stock-based awards***2018 Stock option and grant plan***

The Company's 2018 Stock Option and Grant Plan (the "2018 Plan") provided for the Company to grant incentive stock options or nonqualified stock options, restricted stock awards and other stock-based awards to employees, directors and consultants of the Company. The 2018 Plan was administered by the board of directors or, at the discretion of the board of directors, by a committee of the board of directors. The exercise prices, vesting and other restrictions were determined at the discretion of the board of directors, or its committee if so delegated.

The total number of shares of common stock that could have been issued under the 2018 Plan was 3,071,960 shares, of which 107,635 shares remained available for grant on June 18, 2019, the date that the Company's 2019 Stock Option and Incentive Plan (the "2019 Plan") became effective. Upon the effectiveness of the 2019 Plan, the 107,635

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remaining shares available under the 2018 Plan were transferred and became available for issuance under the 2019 Plan. Shares of common stock underlying outstanding awards under the 2018 Plan that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by the Company prior to vesting, satisfied without the issuance of stock, expire or are otherwise terminated (other than by exercise) will be added to the shares of common stock available for issuance under the 2019 Plan.

2019 Stock option and incentive plan

The 2019 Plan was adopted and approved by the Company's board of directors in May 2019 and by the Company's stockholders in June 2019. The 2019 Plan became effective on June 18, 2019 and replaced the Company's 2018 Plan on that date. The 2019 Plan allows the board of directors or the compensation committee of the board of directors to make equity-based incentive awards to the Company's officers, employees, directors or other key persons (including consultants). The number of shares initially reserved for issuance under the 2019 Plan was 2,572,457, which included the 107,635 shares transferred from the 2018 Plan, and shall be cumulatively increased on each January 1 by 4% of the number of shares of the Company's common stock outstanding on the immediately preceding December 31 or such lesser number of shares determined by the Company's board of directors or compensation committee of the board of directors. The 2019 Plan was increased by 1,396,029 shares on January 1, 2022 and by 1,874,608 shares on January 1, 2023.

The 2019 Plan is administered by the board of directors or, at the discretion of the board of directors, by a committee of the board of directors. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, or its committee if so delegated, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the share of common stock on the date of grant and the term of stock option may not be greater than ten years. All incentive options granted to any person possessing more than 10% of the total combined voting power of all classes of shares may not have an exercise price of less than 110% of the fair market value of the common stock on the grant date. Stock options granted to employees, officers, members of the board of directors and consultants will typically vest over a four-year period.

Shares that are expired, terminated, surrendered or canceled under the 2019 Plan without having been fully exercised will be available for future awards.

2019 Employee stock purchase plan

The 2019 Employee Stock Purchase Plan (the "2019 ESPP") was adopted and approved by the Company's board of directors in May 2019 and by the Company's stockholders in June 2019. The 2019 ESPP became effective on June 18, 2019, at which time 273,869 shares were reserved for issuance. The 2019 ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2020 and each January 1 through January 1, 2029, by the least of (i) 1% of the outstanding number of shares of the Company's common stock on the immediately preceding December 31, (ii) 410,803 shares or (iii) such number of shares as determined by the compensation committee. The 2019 ESPP was increased by 349,007 shares on January 1, 2022 and by 410,803 shares on January 1, 2023.

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Stock option valuation

The assumptions that the Company used to determine the grant-date fair value of stock options granted to employees, directors and consultants as follows, presented on a weighted average basis:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Expected term (in years)	5.85	6.03	5.88	4.86
Expected volatility	79.75 %	74.20 %	78.37 %	73.18 %
Weighted average risk-free interest rate	4.18 %	2.90 %	3.91 %	1.90 %
Expected dividend yield	0.00 %	0.00 %	0.00 %	0.00 %

Stock options

The following table summarizes the Company's stock option activity since December 31, 2022:

	Number of Options	Weighted- Average Exercise Price per Share	Weighted- Average remaining contractual term (years)	Aggregate Intrinsic Value (000's)
Balance outstanding, December 31, 2022	5,780,004	\$ 18.88	7.80	\$ 207,611
Options granted	505,984	\$ 47.45		
Options exercised	(535,387)	\$ 5.39		
Options cancelled	—			
Balance outstanding, September 30, 2023	<u>5,750,601</u>	\$ 22.65	7.42	<u>\$ 160,636</u>
Vested and expected to vest, September 30, 2023	<u>5,750,601</u>	\$ 22.65	7.42	<u>\$ 160,636</u>
Exercisable, September 30, 2023	<u>3,963,342</u>	\$ 17.52	6.86	<u>\$ 131,032</u>

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock.

The weighted average grant-date fair value per share of stock options granted during the three months ended September 30, 2023 and 2022 was \$46.01 and \$6.78, respectively. Additionally, the weighted average grant-date fair value per share of stock options granted during the nine months ended September 30, 2023 and 2022 was \$47.45 and \$11.17, respectively.

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Awards with performance-based vesting conditions granted under the 2019 Plan

In December 2021, the Company granted 610,546 stock options to management at an exercise price of \$21.10, which would vest upon the achievement on or before December 31, 2022 of three pre-determined milestones regarding progress related to the HARMONY study, progress related to the SYMMETRY study, and progress related to availability of drug product for use in Phase 3 clinical trials. One-third of the options were to vest upon achievement of each of the milestones. In January 2022, the Company granted an additional 248,376 stock options to Company employees with the same performance-based milestones and vesting terms at an exercise price of \$21.70. In September 2022, two of the three performance-based awards milestones were achieved and were deemed vested. In December 2022, the third portion of the performance-based awards milestones was achieved and was deemed vested. During the three and nine months ended September 30, 2023, the Company did not have any outstanding performance awards or recognize any performance-based stock compensation expense.

Restricted Stock Units

The 2019 Plan allows for the grants of Restricted Stock Units ("RSUs"). Generally, the RSUs are subject to a four-year vesting period, vesting in equal quarterly installments over the vesting period. In December 2022, the Company granted 129,131 RSUs to executive management with a total grant date fair value of \$5,546. In 2023, The Company granted 41,363 RSUs to executive and non-executive employees with a total grant date fair value of \$1,992. The following table summarizes the Company's RSUs activity since December 31, 2022:

	Underlying shares	Weighted- Average Grant Date Fair Value per Share	Weighted- Average remaining contractual term (years)	Aggregate Intrinsic Value (000's)
Balance outstanding, December 31, 2022	129,131	\$ 42.95	2.07	\$ 7,076
Granted	41,363	\$ 48.17		
Vested	(27,996)	\$ 43.83		
Cancelled or forfeited	—	\$ —		
Balance outstanding, September 30, 2023	<u>142,498</u>	<u>\$ 44.29</u>	1.69	<u>\$ 7,208</u>

The weighted average grant-date fair value per share of RSUs granted during the three months ended September 30, 2023 and 2022 was \$44.52 and \$0, respectively. The weighted average grant-date fair value per share of RSUs granted during the nine months ended September 30, 2023 and 2022 was \$48.17 and \$0, respectively.

Stock-based compensation

The following table summarizes the Company's stock-based compensation expense during the three and nine months ended September 30, 2023 and 2022:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Classified within research and development expense	\$ 1,986	\$ 4,195	\$ 5,485	\$ 6,780
Classified within general and administrative expense	3,753	7,536	9,896	12,423
Total stock-based compensation expense	<u>\$ 5,739</u>	<u>\$ 11,731</u>	<u>\$ 15,381</u>	<u>\$ 19,203</u>

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As of September 30, 2023, total unrecognized compensation cost related to unvested stock options and RSUs was \$38,933 and \$6,110, respectively. These unvested stock options and RSUs are expected to be recognized over a weighted average period of 2.33 years and 3.25 years, respectively.

9. Amgen license agreement

In June 2018, the Company entered into a license agreement (the “Amgen Agreement”) with Amgen, Inc. (“Amgen”) pursuant to which the Company was granted an exclusive license to certain patents and intellectual property related to a long-acting FGF21 analog in order to commercially develop, manufacture, use and distribute FGF21 as a treatment for NASH/MASH and other serious metabolic diseases. The Amgen Agreement provides the Company with exclusive global rights to the licensed products and the right to grant sublicenses that cover EFX to third parties.

In exchange for these rights, the Company made an upfront payment of \$5,000 and issued 2,653,333 shares of Series A Preferred Stock with a fair value of \$1,353 to Amgen. Amgen was also entitled to maintain a 10% ownership interest of the outstanding shares of the Company’s common stock, on a fully diluted and converted basis, through the second closing of the Company’s Series A Preferred Stock financing. In November 2018, in connection with the second closing of the Company’s Series A Preferred Stock financing, the Company issued 3,205,128 shares of Series A Preferred Stock to Amgen for a total value of \$7,404, satisfying its anti-dilution obligation under the Amgen Agreement.

Under the Amgen Agreement, the Company made a milestone payment in the third quarter of 2019 of \$2,500 in connection with dosing the first patient in the BALANCED study and is obligated to pay Amgen \$7,500 in connection with dosing the first patient in a Phase 3 clinical trial, up to \$30,000 in connection with marketing approvals, and aggregate milestone payments of up to \$75,000 upon the achievement of specified commercial milestones for all products licensed under the Amgen Agreement.

Under the Amgen Agreement, the Company is obligated to pay Amgen tiered royalties ranging from a low to high single-digit percentages on annual net sales of the licensed products, beginning on the first commercial sale of such licensed products in each country and expiring on a country-by-country basis on the latest of (i) the expiration of the last valid patent claim covering such licensed products in such country, (ii) the loss of regulatory exclusivity in such country, and (iii) ten years after the first commercial sale of such licensed product in such country. The royalty payments are subject to reduction under specified conditions set forth in the Amgen Agreement.

The Company is solely responsible for all development, manufacturing, and commercial activities and costs of the licensed products, including clinical studies or other tests necessary to support the use of a licensed product. The Company is also responsible for costs related to the filing, prosecution and maintenance of the licensed patent rights.

The Amgen Agreement will remain in effect until the expiration of the royalty term in all countries for all licensed products. The Amgen Agreement may be terminated by either party with at least 90 days’ notice in the event of material breach by the other party that remains uncured for 90 days, by either party for insolvency or bankruptcy of the other party and immediately by Amgen if the Company challenges the licensed patents. The Company may also terminate the Amgen Agreement with 90 days’ written notice for discretionary reasons such as scientific, technical, regulatory or commercial issues, as defined in the Amgen Agreement.

During the three and nine months ended September 30, 2023 and 2022, the Company did not record any research and development expense in connection with the Amgen Agreement.

10. Income taxes

During the three and nine months ended September 30, 2023 and 2022, the Company did not record any income tax benefits for the net operating losses incurred or for the research and development tax credits generated in each period

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due to its uncertainty of realizing a benefit from those items. All of the Company's operating losses since inception have been generated in the United States.

On August 16, 2022, the Inflation Reduction Act of 2022 ("IRA") was signed into law. The IRA includes implementation of a new alternative minimum tax, an excise tax on stock buybacks, and significant tax incentives for energy and climate initiatives, among other provisions. The Company is evaluating the provisions included under the IRA and does not expect the provisions to have a material impact to the Company's condensed consolidated financial statements.

Beginning in 2022, the Tax Cuts and Jobs Act of 2017 eliminates the option to deduct research and development expenditures in the period incurred and requires amortization over five years or fifteen years pursuant to IRC Section 174. Although Congress is considering legislation that would defer the amortization requirement to later years, there is no assurance that the requirement to amortize will be repealed or otherwise modified.

In general, for taxable years beginning on or after January 1, 2015, California law conforms to the IRC as of January 1, 2015. California has not conformed to the federal changes made to the IRC by the Tax Cuts and Jobs Act (Public Law 115-97, enacted on December 22, 2017). In the context of IRC 174, California allows taxpayers to immediately expense R&D costs or capitalize and amortize R&D expenditures over a 5-year recovery period. Thus, the new requirements to capitalize R&D will have no material impact on the state income tax provision.

11. Net loss per share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows:

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2023</u>	<u>2022</u>	<u>2023</u>	<u>2022</u>
Numerator:				
Net loss	\$ (39,659)	\$ (35,542)	\$ (96,573)	\$ (88,974)
Denominator:				
Weighted average common shares outstanding, basic and diluted	55,613,120	38,663,469	51,506,766	36,364,284
Net loss per share, basic and diluted	\$ (0.71)	\$ (0.92)	\$ (1.87)	\$ (2.45)

The Company's potentially dilutive securities, which include stock options, warrants and unvested restricted stock units, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share is the same. The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	<u>Three and nine months ended September 30,</u>	
	<u>2023</u>	<u>2022</u>
Options to purchase common stock	5,750,601	5,390,277
Unvested restricted stock units	142,498	—
Warrants to purchase common stock	45,898	36,718
Warrants available for future grant	137,700	146,880
	<u>6,076,697</u>	<u>5,573,875</u>

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12. Commitments and contingencies

Operating lease

In February 2020, the Company entered into a seven-year agreement to occupy 6,647 square feet of office space in South San Francisco, California. The lease commenced on July 10, 2020 when the Company took occupancy of the leased space and the lease was determined to be operating classified. Under the agreement, the Company is required to make approximately \$2,300 in total minimum payments during the term. The Company is also required to pay its proportionate share of building operating and tax costs after the first year under lease which are not included in the measurement of the lease and treated as variable lease cost and expensed when incurred.

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As of September 30, 2023, maturities of the Company's operating lease liability was as follows:

2023 (remaining)	\$	82
2024		331
2025		341
2026		351
2027		208
Total future minimum lease payments		1,313
Less imputed interest		(173)
Present value of operating lease liabilities	\$	1,140

As of September 30, 2023, the total lease liability was \$1,140, of which \$888 was noncurrent and \$252 was short-term and classified within "Accrued expenses and other current liabilities" on the condensed consolidated balance sheet.

For the three and nine months ended September 30, 2023 and 2022, the components of operating lease cost were as follows:

	Statement of Operations Classification:	Three Months Ended September 30,		Nine Months Ended September 30,	
		2023	2022	2023	2022
Lease cost:					
Operating lease cost	General and administrative expense	\$ 81	\$ 81	\$ 243	\$ 243
Short-term lease cost	General and administrative expense	36	—	125	29
Variable operating lease cost	General and administrative expense	8	9	27	52
Total operating lease cost		\$ 125	\$ 90	\$ 395	\$ 324
Other information:					
Cash paid for amounts included in the measurement of operating lease liability		\$ 81	79	\$ 240	\$ 233
Weighted average remaining lease term (years)		3.8	4.8	3.8	4.8
Weighted average discount rate		7.6%	7.6%	7.6%	7.6%

Research and manufacturing and other commitments

The Company has entered into agreements with contract research organizations and contract manufacturing organizations to provide services in connection with its nonclinical studies and clinical trials and to manufacture clinical development materials. As of September 30, 2023, the Company had non-cancelable purchase and other commitments under these agreements totaling \$21,083.

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Indemnification agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and its executive officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not currently aware of any indemnification claims and has not accrued any liabilities related to such obligations in its condensed consolidated financial statements as of September 30, 2023.

Legal proceedings

The Company is not a party to any litigation and does not have contingency reserves established for any litigation liabilities. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses as incurred the costs related to such legal proceedings.

13. Subsequent event

The Company evaluated subsequent events through November 13, 2023, the date on which these condensed consolidated financial statements were issued. Based on this evaluation, it was determined that no subsequent events occurred that require recognition or disclosure in its financial statements for the three months and nine months ended September 30, 2023.

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

The following discussion should be read in conjunction with our financial statements and accompanying footnotes appearing elsewhere in this Quarterly Report on Form 10-Q and the audited financial statements and related notes contained in our Annual Report on Form 10-K for the year ended December 31, 2022. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. See "Special Note Regarding Forward-Looking Statements." Because of many factors, including those factors set forth in the "Risk Factors" section of this Quarterly Report on Form 10-Q, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Overview

We are a clinical-stage company dedicated to developing transformational treatments for patients with serious metabolic diseases marked by high unmet medical need, including metabolic dysfunction-associated steatohepatitis ("NASH/MASH"), a disease without any approved therapies. NASH/MASH is a severe form of metabolic dysfunction-associated steatotic liver disease ("MASLD"), characterized by inflammation and fibrosis in the liver that can progress to cirrhosis, liver failure, cancer and death. Our lead product candidate, efruxifermin ("EFX"), is an analog of fibroblast growth factor 21 ("FGF21"), which is an endogenously expressed hormone that protects against cellular stress and regulates metabolism of lipids, carbohydrates and proteins throughout the body. Based on statistically significant response rates for fibrosis regression among patients with biopsy-confirmed pre-cirrhotic NASH/MASH and a positive trend observed for fibrosis regression among patients with compensated cirrhosis due to NASH, statistically significant response rates for NASH resolution among patients with biopsy-confirmed pre-cirrhotic NASH/MASH and among patients with biopsy-confirmed compensated cirrhosis due to NASH/MASH, and substantial consistency in results across multiple clinical trials on numerous other non-invasive endpoints, we believe EFX has the potential, if approved, to be an important medicine for treating NASH/MASH. A multi-trial Phase 3 program named SYNCHRONY has been initiated, with screening of two of the trials beginning in September 2023.

Results from five randomized, double-blind, placebo-controlled clinical trials evaluating EFX have been reported, and across all trials reported to date a total of 385 adult patients with either NASH/MASH and/or T2D have been treated with EFX and evaluated for up to 96 weeks. An additional 50 healthy overweight volunteers were treated with EFX as part of a Phase 1 biocomparison study.

In the third quarter of 2022, we reported Week 24 results of the 96-week Phase 2b HARMONY study in patients with pre-cirrhotic NASH/MASH (F2-F3) fibrosis. Both the 50mg and 28mg EFX dose groups achieved statistical significance on primary and secondary histology endpoints after 24 weeks. On the primary endpoint of at least a one-stage improvement of fibrosis without worsening of NASH, the 50mg group (41%) and 28mg group (39%) had a response rate approximately double that of placebo (20%). In addition, 76% of patients treated with 50mg EFX and 47% of those treated with 28mg achieved NASH resolution without worsening of fibrosis, which represented response rates approximately three to five times the placebo rate of 15%. We also observed 41% and 29% response rates for the 50mg and 28mg dose groups, respectively, on a combined endpoint of at least a one-stage improvement in fibrosis and NASH resolution, which were approximately six to eight times the 5% placebo rate. Significant improvements in non-invasive fibrosis markers, liver fat, liver enzymes, lipoproteins, and glycemic control were also observed for both EFX dose groups, with an additional significant reduction in body weight observed for the 50mg dose group. Across EFX groups, the most frequent adverse events were gastrointestinal, and mainly of mild severity. We believe these results favorably differentiate EFX within the NASH/MASH landscape.

In the fourth quarter of 2023 we reported Week 36 results of the 96-week Phase 2b SYMMETRY study in patients with biopsy-confirmed compensated cirrhosis due to NASH/MASH (F4, Child-Pugh class A) or cryptogenic cirrhosis presumed secondary to NASH/MASH. Although statistical significance was not achieved on the primary endpoint of fibrosis improvement at 36 weeks, a numerical trend was observed with 22% and 24% of the 28mg and 50mg EFX-treated groups, respectively, experiencing at least a one-stage improvement in liver fibrosis and no worsening of NASH, compared with 14% for placebo. In addition, 4% of patients in each of the EFX-treated groups experienced a three- or two-stage fibrosis improvement (i.e., from compensated cirrhosis (F4) to F1 or F2) without

worsening of NASH, compared with 0% for placebo. Statistically significant rates of NASH resolution were observed in 67% and 60% of patients at week 36 were observed for the 28mg and 50mg EFX-treated groups, respectively, compared with 26% for placebo. Although no head-to-head comparative studies have been conducted, these response rates represent the highest reported to date for NASH resolution in this patient population. Statistically significant improvements were also observed for both EFX groups in non-invasive markers of liver injury and fibrosis, insulin sensitization and lipoproteins. In addition, EFX was reported to be generally well-tolerated.

The SYMMETRY study included an expansion cohort, known as Cohort D, which evaluated the safety and tolerability of EFX compared to placebo when added to an existing GLP-1 receptor agonist in patients with pre-cirrhotic NASH/MASH (F1-F3 fibrosis) and Type 2 diabetes. In June 2023, the Company reported positive topline results from Cohort D, including that patients treated with EFX 50mg for 12 weeks combined with GLP-1 achieved a statistically significant 65% relative reduction in liver fat, compared to a 10% relative reduction for GLP-1 alone and that 88% of patients treated with EFX combined with GLP-1 had normalized liver fat at week 12, a statistically significant difference relative to 10% of those treated with GLP-1 alone. EFX was reported to be generally well tolerated in Cohort D with comparable results for the EFX (N=21) and placebo (N=10) groups and the overall tolerability profile was similar to that observed in our BALANCED and HARMONY studies.

The FDA has granted Fast Track designation and Breakthrough Therapy Designation for EFX for the treatment of NASH/MASH, while the EMA has granted Priority Medicines ("PRIME") designation. The Fast Track and PRIME programs are designed to enhance regulatory support for the development of promising investigational medicines for which early clinical data suggest the potential to meet a high unmet medical need. The FDA's Breakthrough Therapy Designation is designed to expedite development and review of a therapy for a serious or life-threatening disease or condition when preliminary clinical evidence indicates the drug may demonstrate substantial improvement on one or more clinically significant endpoints over available treatments. Benefits of these programs may include more frequent regulatory interactions, enhanced guidance on the overall development plan and regulatory strategy, and accelerated assessment of marketing authorization ("MA") applications.

Supported by data from five separate clinical trials in patients with NASH/MASH and/or T2D, we believe EFX has a unique ability to reproduce the actions of native FGF21. Consequently, we believe EFX holds the potential to be a highly differentiated, important FGF21 analog and promising monotherapy for the treatment of NASH/MASH, if approved. NASH/MASH is a complex disease, and its ideal treatment would include intervening at each stage of its pathogenesis. We believe EFX could potentially address all stages of NASH/MASH pathogenesis in a single treatment: reversing fibrosis, resolving steatohepatitis, and helping to restore healthy metabolism to the whole body. We also believe EFX may be able to be used in combination with other therapies for a potentially greater effect in certain subpopulations, particularly among the substantial proportion of patients with both NASH/MASH and T2D who are expected to be treated with GLP-1 therapeutics to manage their weight and T2D.

Screening for a multi-trial Phase 3 program called SYNCHRONY began in September 2023. The planned Phase 3 program consists of three trials, SYNCHRONY Histology, SYNCHRONY Real-World, and SYNCHRONY Outcomes. We expect to enroll the first patients into SYNCHRONY Histology and SYNCHRONY Real-World during December 2023. SYNCHRONY Histology will evaluate the efficacy of 28 and 50mg doses of EFX in patients with biopsy confirmed pre-cirrhotic NASH/MASH, with fibrosis stage 2 or 3 (F2-F3). The primary endpoint is ≥ 1 -stage fibrosis improvement and resolution of NASH. SYNCHRONY Real-World will assess the safety and tolerability of EFX in patients with non-invasively diagnosed NASH/MASH or MASLD. Key secondary endpoints for each of SYNCHRONY Histology and SYNCHRONY Real-World will include change in biomarkers of fibrosis and other established non-invasive endpoints. A Type B, End-of-Phase 2 meeting request was submitted to FDA in October 2023 to review the Week 36 results of the Phase 2b SYMMETRY study. We expect to finalize the design of the third Phase 3 clinical trial within the SYNCHRONY program, SYNCHRONY Outcomes, after conferring with the FDA during this Type B meeting. SYNCHRONY Outcomes is currently planned, subject to further dialogue with regulatory authorities, to evaluate the efficacy and safety of EFX in a compensated cirrhotic population, for which the primary endpoint will be clinical outcomes, with a cohort of patients evaluated for a histology endpoint that may be submitted together with results from the SYNCHRONY Real-World study for marketing approval. Feedback from regulatory authorities in connection with the Week 36 SYMMETRY results could result in changes to the planned design or lead and/or timing of the SYNCHRONY program.

We were incorporated in January 2017 and have devoted substantially all of our efforts to organizing and staffing our company, business planning, raising capital, in-licensing rights to EFX, research and development activities for EFX, building our intellectual property portfolio, exploring pipeline expansion opportunities, and providing general and administrative support for these operations. To date, we have principally raised capital through the sale of redeemable convertible preferred stock, the initial public offering of our common stock in June 2019, and the sales of common stock in equity offerings, including a \$25.0 million equity investment from Pfizer, Inc., in 2020, 2022 and 2023. We have also borrowed \$25.0 million from a Term Loan provided by Hercules. We have incurred significant operating losses since inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of EFX and any future product candidates. Our net losses were \$96.6 million and \$89.0 million for the nine months ended September 30, 2023 and 2022, respectively. Our net losses were \$112.0 million and \$100.8 million for the years ended December 31, 2022 and 2021, respectively. As of September 30, 2023, we had an accumulated deficit of \$518.9 million.

We expect to continue to incur significant expenses for at least the next several years as we advance EFX through later-stage clinical development, develop additional product candidates and seek regulatory approval of any product candidates that complete clinical development. In addition, if we obtain marketing approval for any product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution.

We may also incur expenses in connection with the in-licensing or acquisition of additional product candidates. As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings, or other capital sources, which may include collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, reduce or eliminate the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of September 30, 2023, we had cash, cash equivalents, short-term and long-term marketable securities of \$613.0 million. Taken together, we believe this will be sufficient to fund our current operating plan into 2026.

Components of our results of operations

Revenue

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of products in the near future, if at all. If our development efforts for EFX or additional product candidates that we may develop in the future are successful and result in marketing approval or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from such collaboration or license agreements.

Operating expenses

Research and development expenses

Research and development expenses consist primarily of costs incurred in connection with the development of EFX, as well as unrelated discovery program expenses. We expense research and development costs as incurred. These expenses include:

- employee-related expenses, including salaries, related benefits and stock-based compensation expense for employees engaged in research and development functions;
- expenses incurred under agreements with CROs that are primarily engaged in the oversight and conduct of our clinical trials; CMOs that are primarily engaged to provide drug substance and product for our clinical trials, research and development programs; as well as investigative sites and consultants that conduct our clinical trials, nonclinical studies and other scientific development services;
- the cost of acquiring and manufacturing nonclinical and clinical trial materials, including manufacturing registration and validation batches;
- costs related to compliance with quality and regulatory requirements; and
- payments made under third-party licensing agreements.

Advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

Product candidates in later stages of clinical development, such as EFX, generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will increase substantially in connection with our planned clinical development activities in the near term and in the future. At this time, we cannot precisely estimate or know the nature, timing and costs of the efforts that will be necessary to complete the clinical development of EFX and any future product candidates.

Our clinical development costs may vary significantly based on factors such as:

- per patient trial costs;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients enrolled in clinical trials;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- any setbacks or delays to the initiation or completion of preclinical or non-clinical studies, product development or clinical trials;
- the cost and timing of manufacturing our product candidates, including on account of any disruption or delays to the supply of our product candidates;
- the phase of development of our product candidates; and
- the efficacy and safety profile of our product candidates.

The successful development and commercialization of product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the following:

- the timing and progress of nonclinical and clinical development activities;
- the number and scope of nonclinical and clinical programs we decide to pursue;
- the ability to raise necessary additional funds;
- the progress of the development efforts of parties with whom we may enter into collaboration arrangements;
- our ability to maintain our current development program and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the successful initiation and completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- the receipt and related terms of regulatory approvals from applicable regulatory authorities;
- the availability of drug substance, drug product, and delivery devices utilized in the production of our product candidates;

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- establishing and maintaining agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if our product candidates are approved;
- our ability to obtain and maintain patents, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- our ability to protect our rights in our intellectual property portfolio;
- the commercialization of our product candidate, if and when approved;
- obtaining and maintaining third-party insurance coverage and adequate reimbursement;
- the acceptance of our product candidate, if approved, by patients, the medical community and third-party payors;
- competition with other products;
- the impacts of a future pandemic, epidemic or outbreak of an infectious disease, such as COVID-19, on the supply of our product candidate and ability to successfully initiate and complete preclinical and non-clinical studies and clinical trials, to receive regulatory approval for our product candidate and to commercialize our product candidate, if approved; and
- a continued acceptable safety profile of our therapies following any approval.

A change in the outcome of any of these variables with respect to the development of our product candidates could significantly change the costs and timing associated with their development. We may never succeed in obtaining regulatory approval for any of our product candidates.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related costs for personnel in executive, finance, corporate and business development, and administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters; professional fees for accounting, auditing, tax and administrative consulting services; insurance costs; administrative travel expenses; marketing expenses and other operating costs.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support development of EFX and our continued research activities. We also anticipate that we will incur increased accounting, audit, legal, tax, regulatory, compliance, and director and officer insurance costs, as well as investor and public relations expenses associated with maintaining compliance with exchange listing and SEC requirements.

Interest expense

Interest expense consists primarily of interest expense on our term loan with Hercules.

Other income

Other income consists primarily of interest income earned on our cash, cash equivalents and short and long-term marketable securities.

Results of operations**Comparison of the three months ended September 30, 2023 and 2022**

The following table summarizes our results of operations for the three months ended September 30, 2023 and 2022:

	Three Months Ended September 30,		\$ Change	% Change
	2023	2022		
	(in thousands, except percentages)			
Operating expenses:				
Research and development	\$ 38,634	\$ 25,087	\$ 13,547	54 %
General and administrative	7,981	11,004	(3,023)	(27) %
Total operating expenses	46,615	36,091	10,524	29 %
Loss from operations	(46,615)	(36,091)	(10,524)	29 %
Interest expense	(888)	(324)	(564)	174 %
Other income, net	7,844	873	6,971	799 %
Net loss	\$ (39,659)	\$ (35,542)	\$ (4,117)	12 %

Research and development expenses

The following table summarizes our research and development expenses incurred during the three months ended September 30, 2023 and 2022:

	Three Months Ended September 30,		\$ Change	% Change
	2023	2022		
	(in thousands, except percentages)			
Research and development expenses:				
Direct EFX program expenses	\$ 32,943	\$ 18,873	\$ 14,070	75 %
Personnel and other R&D related expenses	5,691	6,214	(523)	(8) %
Total research and development expenses	\$ 38,634	\$ 25,087	\$ 13,547	54 %

Research and development expenses were \$38.6 million and \$25.1 million for the three months ended September 30, 2023 and 2022, respectively, an increase of \$13.5 million. Direct costs for our EFX program increased \$14.1 million, attributed primarily to a \$7.8 million increase in third-party contract manufacturing expenses for EFX, a \$7.0 million increase in CRO expenses related to our ongoing HARMONY and SYMMETRY clinical trials, offset by a \$0.7 million decrease in other research and development costs. Personnel and other research and development expenses decreased \$0.5 million, due to a \$1.7 million increase in wage and wage-related expenses resulting from increased staff, offset by a \$2.2 million decrease in stock-based compensation. We expect that our research and development expenses will increase substantially in connection with our planned manufacturing and clinical development activities in the near term and in the future.

General and administrative expenses

General and administrative expenses were \$8.0 million and \$11.0 million for the three months ended September 30, 2023 and 2022, respectively, a decrease of \$3.0 million, which was due primarily to a \$0.7 million increase in wage, wage-related and third party consulting expenses, offset by a \$3.8 million decrease in stock-based compensation.

Interest expense was \$0.9 million and \$0.3 million for the three months ended September 30, 2023 and 2022, respectively, an increase of \$0.6 million related to the Hercules term loan.

Other income, net

Other income, net was \$7.8 million and \$0.9 million for the three months ended September 30, 2023 and 2022, respectively, an increase of \$7.0 million which was due primarily to a \$6.9 million increase in interest income from our investment portfolio.

Comparison of the nine months ended September 30, 2023 and 2022

The following table summarizes our results of operations for the nine months ended September 30, 2023 and 2022:

	Nine Months Ended September 30,		\$ Change	% Change
	2023	2022		
(in thousands, except percentages)				
Operating expenses:				
Research and development	\$ 88,406	\$ 66,964	\$ 21,442	32 %
General and administrative	22,591	22,772	(181)	(1) %
Total operating expenses	110,997	89,736	21,261	24 %
Loss from operations	(110,997)	(89,736)	(21,261)	24 %
Interest expense	(2,202)	(377)	(1,825)	484 %
Other income, net	16,626	1,139	15,487	1,360 %
Net loss	\$ (96,573)	\$ (88,974)	\$ (7,599)	9 %

Research and development expenses

The following table summarizes our research and development expenses incurred during the nine months ended September 30, 2023 and 2022:

	Nine Months Ended September 30,		\$ Change	% Change
	2023	2022		
(in thousands, except percentages)				
Research and development expenses:				
Direct EFX program expenses	\$ 72,931	\$ 54,110	\$ 18,821	35 %
Personnel and other R&D related expenses	15,475	12,854	2,621	20 %
Total research and development expenses	\$ 88,406	\$ 66,964	\$ 21,442	32 %

Research and development expenses were \$88.4 million and \$67.0 million for the nine months ended September 30, 2023 and 2022, respectively, an increase of \$21.4 million. Direct costs for our EFX program increased by \$18.8 million, attributed primarily to a \$10.3 million increase in CRO expenses related to our ongoing HARMONY and SYMMETRY clinical trials and a \$9.3 million increase in third-party contract manufacturing expenses for EFX, offset by a \$0.8 million decrease in other research and development expenses. Personnel and other research and development expenses increased \$2.6 million, due to a \$3.9 million increase in wage and wage-related expenses resulting from increased staff offset by a \$1.3 million decrease in stock-based compensation. We expect that our research and development expenses will increase substantially in connection with our planned manufacturing and clinical development activities in the near term and in the future.

General and administrative expenses

General and administrative expenses were \$22.6 million and \$22.8 million for the nine months ended September 30, 2023 and 2022, respectively, a decrease of \$0.2 million which was due primarily to a \$1.2 million

increase in wage and wage-related expenses resulting from increased staff and a \$1.1 million increase in third party consulting and other expenses, offset by a \$2.5 million decrease in stock-based compensation.

Interest expense

Interest expense was \$2.2 million and \$0.4 million for the nine months ended September 30, 2023 and 2022, respectively. Interest expense is primarily related to the Hercules term loan.

Other income, net

Other income, net was \$16.6 million and \$1.1 million for the nine months ended September 30, 2023 and 2022, respectively, an increase of \$15.5 million which was due primarily to a \$15.6 million increase in interest income from our investment portfolio.

Liquidity and capital resources

From our inception through September 30, 2023, we have incurred significant operating losses. We have not yet commercialized any products and we do not expect to generate revenue from sales of products for several years, if at all. Through September 30, 2023, we had funded our operations primarily with proceeds from the sale of our redeemable convertible preferred stock, the initial public offering of our common stock in June 2019, and follow-on public offerings of our common stock in July 2020 and in September 2022. In June 2022, we received \$25.0 million from an equity investment from Pfizer, Inc. and \$10.0 million from a Term Loan provided by Hercules. An additional \$15.0 million was borrowed from Hercules on March 10, 2023. In April and May 2023, we received gross proceeds of \$127.4 million in an ATM offering and gross proceeds of \$220.0 million from the sale of common stock in an underwritten registered direct offering. From our inception through September 30, 2023, these and other funding sources have provided gross proceeds totaling \$1,040.2 million. As of September 30, 2023, we had cash, cash equivalents short and long-term marketable securities of \$613.0 million. We have invested our cash resources primarily in liquid money market accounts, U.S Treasuries and agency securities, commercial paper and corporate debt securities.

The following table summarizes our cash flows for the periods indicated:

	Nine Months Ended September 30,	
	2023	2022
	(in thousands)	
Net cash used in operating activities	\$ (96,740)	\$ (67,009)
Net cash (used in) provided by investing activities	(236,409)	37,620
Net cash provided by financing activities	352,814	252,909
Net increase in cash, cash equivalents and restricted cash	<u>\$ 19,665</u>	<u>\$ 223,520</u>

Cash flows from operating activities

Cash used in operating activities for the nine months ended September 30, 2023 was \$96.7 million, consisting of a net loss of \$96.6 million offset by non-cash charges of \$10.4 million, including \$15.4 million of stock-based compensation expense, and a decrease in changes in our operating assets and liabilities of \$10.6 million. The changes in operating assets and liabilities was primarily due to the timing of prepayments and payments to our CMOs and CROs for ongoing clinical trial and manufacturing activities.

Cash used in operating activities for the nine months ended September 30, 2022 was \$67.0 million, consisting of a net loss of \$89.0 million offset by non-cash charges of \$19.7 million, including \$19.2 million of stock-based compensation expense, and changes in our operating assets and liabilities of \$2.3 million. The changes in operating assets and liabilities was primarily due to the timing of prepayments and payments to our CMOs and CROs for ongoing clinical trial and manufacturing activities.

Cash flows from investing activities

Cash used in investing activities for the nine months ended September 30, 2023 was \$236.4 million from the purchases and maturities of short and long-term marketable securities.

Cash provided by investing activities for the nine months ended September 30, 2022 was \$37.6 million from the maturities of short-term marketable securities.

Cash flows from financing activities

Cash provided by financing activities for the nine months ended September 30, 2023 was \$352.8 million, including \$15.0 million from a Term Loan provided by Hercules, \$123.8 million of net proceeds from the ATM offering, \$211.0 million of net proceeds from a registered direct offering and \$2.8 million in proceeds from the exercise of stock options.

Cash provided by financing activities for the nine months ended September 30, 2022 was \$252.9 million, including \$216.2 million from follow-on public offering proceeds, net of underwriting discounts, \$25.0 million from an equity investment from Pfizer, Inc. through a registered direct common stock offering, \$10.0 million from a Term Loan provided by Hercules and \$2.4 million in proceeds from the exercise of stock options and the issuance of employee stock purchase plan shares.

Description of Indebtedness

We have outstanding borrowings of \$25.0 million under a loan and security agreement with Hercules. We may borrow an additional \$10.0 million at our sole discretion until December 15, 2023. Upon the occurrence of certain clinical development milestones, an additional \$20.0 million may become available to us. In addition, up to an additional \$45.0 million may become available to us at Hercules' sole discretion. Borrowings under the loan are repayable in monthly interest-only payments until July 1, 2024, with the option to extend under certain conditions. The interest-only period will be followed by equal monthly payments of principal plus interest until the loan maturity date of January 1, 2027. Outstanding borrowings bear interest at the greater of (i) 7.65% and (ii) the prime rate as reported in the Wall Street Journal plus 3.65%.

Funding requirements

Our primary uses of capital are, and we expect will continue to be, research and development services, compensation and related expenses and general overhead costs. We expect to continue to incur significant expenses and operating losses for the foreseeable future. In addition, since the closing of our IPO, we have incurred and expect to continue to incur additional costs associated with operating as a public company. We anticipate that our expenses will increase significantly in connection with our ongoing activities. The timing and amount of our operating expenditures will depend largely on:

- the initiation, progress, timing, costs and results of nonclinical studies and clinical trials for EFX or any future product candidates we may develop;
- timing delays, if any, with respect to preclinical and clinical development of EFX or any future product candidates we may develop as a result of a pandemic, epidemic or outbreak of an infectious disease;
- our ability to maintain our license to EFX from Amgen;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more nonclinical studies or clinical trials than those that we currently expect or change their requirements on studies or trials that had previously been agreed to;
- the cost to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing any patents or other intellectual property rights;
- the effect of competing technological and market developments;

- market acceptance of any approved product candidate, including product pricing, as well as product coverage and the adequacy of reimbursement by third-party payors;
- the cost of acquiring, licensing or investing in additional businesses, products, product candidates and technologies;
- the cost and timing of selecting, auditing and potentially validating a manufacturing site for commercial scale manufacturing;
- the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval and that we determine to commercialize; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems.

We expect that we will require additional funding to complete the clinical development of EFX, commercialize EFX, if we receive regulatory approval, and pursue in-licenses or acquisitions of other product candidates. If we receive regulatory approval for EFX or other product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on whether we choose to commercialize EFX ourselves.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and marketing, distribution or licensing arrangements with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership interest may be materially diluted, and the terms of such securities could include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, reduce or eliminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual obligations and other commitments

During the three and nine months ended September 30, 2023, there have been no material changes outside the ordinary course of business to our contractual obligations and commitments from those disclosed in Management's Discussion and Analysis of Financial Condition and Results of Operations, set forth in Part II, Item 7, of our Annual Report on Form 10-K for fiscal year 2022, other than the Term Loan to Hercules Capital, Inc. discussed in Part I, Item 1, Footnote 6 to the Unaudited Condensed Consolidated Financial Statements of this Quarterly Report on Form 10-Q and to changes in our non-cancelable purchase arrangements.

Non-cancelable purchase and other arrangements increased to \$22.4 million as of September 30, 2023, compared to \$8.8 million as of December 31, 2022. The increase of \$13.6 million was primarily attributable to \$13.8 million increase in the purchase obligations to support the growth and expansion of our clinical trials activities, offset by a \$0.2 million decrease in operating lease obligations for the office space in South San Francisco, California.

Critical accounting policies and estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with United States generally accepted accounting principles. The preparation of our financial statements and related disclosures requires us to make estimates, assumptions and judgments that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. Our critical accounting policies are described under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Significant Judgments and Estimates" in our Annual Report on Form 10-K for the year ended December 31, 2022 which was filed with the Securities and Exchange Commission on March 17, 2023. There were no material changes to our critical accounting policies through September 30, 2023 from those discussed in our Annual Report on Form 10-K for the year ended December 31, 2022.

Recent accounting pronouncements

See Note 2 to our unaudited condensed consolidated financial statements included in Part I, Item 1, “Notes to Unaudited Condensed Consolidated Financial Statements,” of this Quarterly Report on Form 10-Q for a description of recent accounting pronouncements applicable to our business.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Risk

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents, short and long-term marketable securities of \$613.0 million as of September 30, 2023, which consisted primarily of money market funds and U.S. Treasury-backed securities which are investment grade.

The primary objective of our investment activities is to preserve capital to fund our operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of investments in a variety of securities of high credit quality and short and long-term duration, according to our board-approved investment policy. Our investments are subject to interest rate risk and could fall in value if market interest rates increase.

Additionally, the Company has a variable interest rate term loan that is impacted by the increase in interest rates. A hypothetical 10% relative change in interest rates during any of the periods presented would not have a material impact on our condensed consolidated financial statements.

Foreign Currency Risk

The majority of our transactions occur in U.S. dollars. However, we do have certain transactions that are denominated in currencies other than the U.S. dollar, primarily the Euro and British Pound, and we therefore are subject to foreign exchange risk. The fluctuation in the value of the U.S. dollar against other currencies affects the reported amounts of expenses, assets and liabilities primarily associated with a limited number of manufacturing activities. The effect of a hypothetical 10% change in foreign currency exchange rates applicable to our business would not have had a material impact on our historical condensed consolidated financial statements for the three and nine months ended September 30, 2023.

Inflation Risk

Although, we do not believe that inflation has had a material effect on our business, financial position or results of operations to date, we may experience some effect in the near future (especially if inflation rates continue to rise) due to an impact on the costs to conduct clinical trials, manufacturing and supply costs, labor costs we incur to attract and retain qualified personnel, and other operational costs. Inflationary costs could adversely affect our business, financial condition and results of operations.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

As required by Rule 13a-15(b) under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), our management, under the supervision and with the participation of our principal executive officer (our Chief Executive Officer) and our principal financial officer (our Chief Financial Officer), have evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act as of September 30, 2023. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer (our Chief Executive Officer) and our principal financial officer (our Chief Financial Officer), as appropriate, to allow timely decisions regarding required disclosure. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on that evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that, as of the end of September 30, 2023, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the three or nine months ended September 30, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

All control systems have inherent limitations including the realities that judgments in decision making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the controls. Because of such limitations, there is a risk that material misstatements will not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Item 1. Legal Proceedings.

From time to time, we may be involved in lawsuits, claims, investigations and proceedings, consisting of intellectual property, commercial, employment and other matters which arise in the ordinary course of business. While the outcome of any such proceedings cannot be predicted with certainty, as of September 30, 2023, we were not party to any legal proceedings that we would expect to have a material adverse impact on our financial position, results of operations or cash flow.

Item 1A. Risk Factors.

In evaluating the Company and our business, careful consideration should be given to the following risk factors, in addition to the other information set forth in this Quarterly Report on Form 10-Q and in other documents that we file with the SEC. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occur, our business, prospects, financial condition, results of operations and cash flow could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks facing the Company. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition, results of operations or cash flow.

Risks Related to the Clinical Development and Manufacturing of our Product CandidateRisks Related to Clinical Development

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control, including difficulties in identifying patients with NASH/MASH, significant competition for recruiting such patients in clinical trials, and restrictions on patients and investigators related to outbreaks of infectious diseases or public health crises.

Identifying and qualifying patients to participate in clinical trials is critical to our success. We may be unable to retain a sufficient number of patients to successfully complete the long-term follow-up portion of the ongoing Phase 2b HARMONY or SYMMETRY studies, and may encounter delays in enrolling or be unable to enroll or retain a sufficient number of patients in our planned Phase 3 SYNCHRONY studies or any other future clinical trials. In particular, as a result of the inherent difficulties in diagnosing NASH/MASH and the significant competition for recruiting patients with NASH/MASH in clinical trials, there may be delays in enrolling the patients we need to complete clinical trials on a timely basis, or at all. In addition, enrollment in Phase 3 clinical trials may be adversely affected by marketing approval for one or more investigational NASH/MASH drugs.

Factors that may generally affect patient enrollment include:

- the size and nature of the patient population;
- the number and location of clinical sites we enroll;
- the impact of geopolitical tensions, such as the ongoing armed conflict in Israel and the Gaza Strip, on clinical trial sites, such as those in Turkey and Israel, where we are currently planning to activate sites in our Phase 3 SYNCHRONY program;
- the ability of our clinical sites to maintain adequate personnel;
- competition with other companies for clinical sites or patients;
- the eligibility and exclusion criteria for the trial;
- the design of the clinical trial;
- inability to obtain and maintain patient consents;
- risk that enrolled participants will drop out before completion;
- the availability of marketed therapies; and

- clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

In addition, if any significant adverse events or other side effects are observed in any of our future clinical trials, it may make it more difficult for us to recruit patients to our clinical trials and patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of one or more product candidates altogether. Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays, which would increase our costs and have an adverse effect on our company.

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

The biotechnology industry is intensely competitive and subject to rapid and significant technological change. Our competitors include multinational pharmaceutical companies, specialized biotechnology companies and universities and other research institutions. We understand that a number of pharmaceutical companies, including AstraZeneca PLC/MedImmune LLC, Boehringer Ingelheim AG, Inc., Eisai, Inc., Eli Lilly, GSK plc, and Company, Johnson & Johnson, Merck & Co., Inc., Novo Nordisk A/S, Pfizer Inc., Roche Holding AG and Takeda Pharmaceutical Company Limited, as well as large and small biotechnology companies such as Alnylam Pharmaceuticals, Inc., Altimmune, Inc., Amgen, Inc., Arrowhead Pharmaceuticals, Inc., Boston Pharmaceuticals, Inc., Cirius Therapeutics, Inc., CohBar, Inc., 89bio, D&D Pharmatech, Inc., Galectin Therapeutics Inc., Galmed Pharmaceuticals Ltd., Gilead Sciences, Inc., Hanmi Pharmaceutical Company, Ltd., HighTide Therapeutics Inc., Inventiva Pharma SA, Ionis Pharmaceuticals, Inc., Madrigal Pharmaceuticals, Inc., MediciNova, Inc., North Sea Pharmaceuticals, Regeneron Pharmaceuticals, Inc., Poxel SA, Sagimet Biosciences, Inc., Terns Pharmaceuticals, Inc. and Viking Therapeutics, Inc. are or may be pursuing the development or marketing of pharmaceuticals that target NASH/MASH. It is also probable that the number of companies seeking to develop products and therapies for the treatment of serious metabolic diseases, such as NASH/MASH, will increase. Many of our competitors have substantially greater financial, technical, human and other resources than we do and may be better equipped to develop, manufacture and market technologically superior products. In addition, many of these competitors have significantly greater experience than we have in undertaking nonclinical studies and human clinical trials of new pharmaceutical products and in obtaining regulatory approvals of human therapeutic products. Accordingly, our competitors may succeed in obtaining FDA approval for superior products. In addition, many competitors have greater name recognition and more extensive collaborative relationships.

Smaller and earlier-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

Our competitors may obtain regulatory approval of their products more rapidly than we do or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidate or any future product candidates. Our competitors may also develop drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than we are in manufacturing and marketing their products. If we are unable to compete effectively against these companies, then we may not be able to commercialize our product candidate or any future product candidates or achieve a competitive position in the market. This would adversely affect our ability to generate revenue. Our competitors also compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Failures or delays in the commencement or completion of, or ambiguous or negative results from our planned clinical trials of our product candidates could result in increased costs to us and could delay, prevent, or limit our ability to generate revenue and continue our business.

We do not know whether the long-term follow-up portions of the HARMONY study or the SYMMETRY study will be completed or the Phase 3 SYNCHRONY program or any future clinical trials will enroll or be completed on schedule, if at all, as the commencement and completion of clinical trials can be delayed or prevented for a number of reasons, including, among others:

- the FDA or comparable foreign regulatory authorities may not authorize us or our investigators to commence our planned clinical trials or any other clinical trials we may initiate, or may suspend our clinical trials, for example, through imposition of a clinical hold, and may request additional data to permit allowance of our IND;
- delays in filing or receiving allowance of additional INDs that may be required;
- lack of adequate funding to continue our clinical trials and nonclinical studies;
- negative results from our ongoing nonclinical studies;
- delays in reaching or failing to reach agreement on acceptable terms with prospective CROs and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and study sites;
- inadequate quantity or quality of a product candidate or other materials necessary to conduct clinical trials, for example delays in the manufacturing of sufficient supply of finished drug product;
- difficulties obtaining ethics committee or Institutional Review Board ("IRB") approval to conduct a clinical study at a prospective site or sites;
- challenges in recruiting and enrolling subjects to participate in clinical trials, the proximity of subjects to study sites, eligibility criteria for the clinical study, the nature of the clinical study protocol, the availability of approved effective treatments for the relevant disease, and competition from other clinical study programs for similar indications;
- challenges and delays in activating planned clinical trial sites globally due to the impact of geopolitical tensions, including the ongoing armed conflict in Israel and the Gaza Strip;
- severe or unexpected drug-related side effects experienced by subjects in a clinical trial;
- we may decide, or regulatory authorities may require us, to conduct additional nonclinical or clinical trials or abandon product development programs;
- delays in validating, or inability to validate, any endpoints utilized in a clinical trial;
- the FDA or comparable foreign regulatory authorities may disagree with our clinical study 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; and
- difficulties retaining subjects who have enrolled in a clinical trial but may be prone to withdrawal due to rigors of the clinical trials, lack of efficacy, side effects, personal issues, or loss of interest.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical study may be suspended or terminated by us, the FDA or comparable foreign regulatory authorities, the IRBs at the sites where the IRBs are overseeing a clinical study, a data and safety monitoring board ("DSMB") overseeing the clinical study at issue or other regulatory authorities due to a number of factors, including, among others:

- failure to conduct the clinical study in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical study operations or study sites by the FDA or other regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including in response to the imposition of a clinical hold;
- unforeseen safety issues or safety signals, including any that could be identified in our ongoing nonclinical studies or clinical trials, adverse side effects or lack of effectiveness;
- changes in government regulations or administrative actions;
- problems with clinical supply materials; and
- lack of adequate funding to continue clinical trials.

Any inability to successfully complete nonclinical and clinical development could result in additional costs to us or impair our ability to generate revenue. In addition, if we make changes to a product candidate, such as the drug product-device combination that we plan to use in the Phase 3 SYNCHRONY program, we may need to conduct additional nonclinical studies or clinical trials to bridge or demonstrate the comparability of our modified product candidate to earlier versions, which could delay our clinical development plan or marketing approval for our current product candidate and any future product candidates. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Clinical development is uncertain and our clinical trials for EFX and any future product candidates may experience delays, which would adversely affect our ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.

We cannot be sure that we will be able to continue development of EFX or submit INDs or similar applications for any future product candidates, on the timelines we expect, if at all. To proceed with our development plans and ultimately commercialization, we may need to conduct and meet regulatory requirements for additional preclinical studies and clinical trials. We cannot be certain of the timely completion or outcomes of our preclinical testing and studies and cannot predict if the FDA or other regulatory authorities will accept our proposed clinical programs or if the outcomes of our preclinical studies and clinical trials will enable any future clinical trials to begin under a proposed protocol.

We rely and will continue to rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates.

We depend and will continue to depend upon third parties, including independent investigators, to conduct our clinical trials under agreements with universities, medical institutions, CROs, strategic partners and others. We expect to have to negotiate budgets and contracts with CROs and trial sites, which may result in delays to our development timelines and increased costs.

We rely heavily on third parties over the course of our clinical trials, and, as a result, have limited control over the clinical investigators and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol. Nevertheless, our reliance on third parties does not relieve us of our regulatory responsibilities and we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. We and these third parties are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional nonclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, regulatory authorities will determine that any of our clinical trials comply with the GCP requirements. In addition, our clinical trials must be conducted with products produced under current good manufacturing practice ("cGMP") requirements and may require a large number of patients. Our failure or any failure by these third parties to comply with these applicable regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

The third parties who conduct our clinical trials are not our employees and, except for remedies that may be available to us under our agreements with those third parties, we cannot control whether or not they devote sufficient time and resources to our ongoing nonclinical and clinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates in a timely manner or at all. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the clinical data they obtain is compromised due to the failure (including by clinical sites or investigators) to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenues could be delayed significantly.

Risks Related to the Manufacturing of our Product Candidate

We are subject to many manufacturing risks, any of which could substantially increase our costs, delay clinical programs and limit supply of our product candidates.

We have contracted with a third-party manufacturer, Boehringer Ingelheim, to make EFX drug substance (active pharmaceutical ingredient ("API")) and with another third-party manufacturer, Vetter Pharma International GmbH, or Vetter, to manufacture EFX drug product ("DP") including a DP-device combination to be used in Phase 3 studies. We have successfully manufactured API and a DP-device combination under GMP conditions, which have both been released for Phase 3 clinical use. We plan to enter into new commercial supply agreements with each of Boehringer Ingelheim and Vetter at the appropriate time. For Phase 3 clinical studies, the formulation used for API manufacture has been modified to enable production of a lyophilized DP rather than the frozen liquid used in Phase 2b studies. This change improves long-term pharmaceutical stability of the DP, making it suitable as the potential commercial presentation. A program of pharmaceutical and clinical studies has shown that the DP-device presentation to be used in Phase 3 studies is comparable to that used for Ph2b.

The process of manufacturing our product candidates is complex, highly regulated and subject to several risks, including:

- the manufacturing process is susceptible to product loss due to contamination by adventitious microorganisms, equipment failure, improper installation or operation of equipment, vendor or operator error and improper storage conditions. Even minor deviations from normal manufacturing processes could result in reduced production yields and quality as well as other supply disruptions. If microbial, viral, or other contaminants are discovered in our products or in the manufacturing facilities in which our products are made, the manufacturing facilities may need to be closed for an extended period of time to investigate and eliminate the contamination;
- the manufacturing facilities in which our products are made could be adversely affected by equipment failures, labor and raw material shortages, pandemics, epidemics, or outbreaks of infectious disease, financial difficulties of our contract manufacturers, natural disasters, power failures, local political unrest and numerous other factors; and
- any adverse developments affecting manufacturing operations for our products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls or other interruptions in the supply of our products. We may also have to record inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more expensive manufacturing alternatives.

The manufacture of EFX requires significant expertise and capital investment, including the development of advanced manufacturing techniques and in-process controls. Manufacturers of these products sometimes encounter difficulties in production, especially during scale-up from the manufacturing process used for early clinical trials to a validated and qualified process needed for pivotal clinical trials and commercial launch. These problems include failure to meet target production costs and yields, failure to meet product release specifications, including stability of the product, quality assurance system failures, operator error and shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. We cannot assure you that any product quality issues relating to the manufacture of our product candidate or any future product candidates will not occur in the future.

We do not have, and we do not currently plan to acquire or build the facilities or internal capabilities to manufacture bulk drug substance, finished drug product or delivery device for use in clinical trials or commercialization. To a large extent, that makes us dependent on the goodwill of our contract manufacturing partners to quickly fix deviations that will inevitably occur during the manufacturing of our product and to manufacture API and/or the DP-device combination in sufficient quantities to meet commercial demand, if approved for marketing. Any delay or interruption in the supply of clinical trial materials on our contract manufacturing partners, could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials altogether.

A new lyophilized EFX DP-device combination product for commercial use is being evaluated in the Phase 3 SYNCHRONY program. The dual-chamber prefilled syringe is being manufactured by Vetter. cGMP-compliant batches have been released and shipped for the Phase 3 SYNCHRONY program. The corresponding CMC modules of the IND application covering API and DP-device combination have been reviewed by FDA.

We contract with third parties for the manufacture of EFX and the delivery device utilized for EFX and expect to continue to do so for future clinical trials and for commercialization of EFX as well as for any future product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of EFX, or the delivery devices utilized for EFX, or any future product candidates or medicines or that such supply will not be available to us at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third-party manufacturers for the manufacture of EFX, delivery devices utilized for EFX or any future product candidates for nonclinical and clinical testing and for commercial supply of any of these product candidates for which we obtain marketing approval. Reliance on third-party manufacturers may expose us to different risks than if we were to manufacture product candidates ourselves. To the extent any issues arise with our third-party manufacturers, we may be unable to establish any agreements with any other third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance and safety and pharmacovigilance reporting.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. For our product candidates that are biologic-device combination products, third-party manufacturers may not be able to comply with cGMP regulatory requirements applicable to biologic-device combination products, including applicable provisions of the FDA's drug product cGMP regulations, device cGMP requirements embodied in the FDA's Quality System Regulation ("QSR") or similar regulatory requirements outside the United States. Our failure, or the failure of third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or medicines, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business and results of operations.

If any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to or approved by the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our product candidates. In addition, in the case of CMOs that supply our product candidate, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply of bulk drug substance or for the manufacture of our drug product-delivery device combination. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there potentially are alternative manufacturers who could manufacture our drug substance or drug product-delivery device combination or any future product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

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

The manufacture of our product candidates is complex and we may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

The processes involved in manufacturing our product candidates, including pre-filled, dual-chamber syringe presentations of our product candidates, are complex, expensive, highly regulated, and subject to multiple risks. Further, as product candidates are developed through nonclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials.

In addition, the manufacturing process for any products that we may develop is subject to FDA and other comparable foreign regulatory authority approval processes and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA and foreign regulatory authority requirements, including, for example, complying with cGMPs, applicable product tracking and tracing requirements and applicable QSRs, on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce products to specifications acceptable to the FDA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our contract manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging or comparability nonclinical or clinical trials or the repetition of one or more clinical trials, increase clinical study costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations, and growth prospects.

Risks Related to Our Business, Industry and Intellectual Property

Risks Related to Business Development

We are heavily dependent on the success of EFX, our only product candidate.

We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We expect that a substantial portion of our efforts and expenditures over the next several years will be devoted to EFX, which is currently our only product candidate. Accordingly, our business currently depends heavily on the successful development, regulatory approval, and commercialization of EFX. We cannot be certain that EFX will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. If we were required to discontinue development of EFX or if EFX does not receive regulatory approval or fails to achieve significant market acceptance, we would be delayed by many years in our ability to achieve profitability, if ever.

The research, testing, manufacturing, safety, efficacy, labeling, approval, sale, marketing, and distribution of EFX is, and will remain, subject to comprehensive regulation by the FDA and foreign regulatory authorities. Failure to obtain regulatory approval for EFX in the United States, Europe, Japan or other jurisdictions will prevent us from commercializing and marketing EFX in such jurisdictions.

Clinical development of EFX prior to the BALANCED study was conducted by Amgen, Inc. ("Amgen") in patients with T2D. We did not conduct any of the development of EFX related to clinical trials in patients with T2D, and we have relied on Amgen to have conducted such research and development in accordance with the applicable protocol, legal, regulatory, and scientific standards, have accurately reported the results of all nonclinical studies and clinical trials conducted prior to our license of EFX, and have correctly collected and interpreted the data from these studies and trials. To the extent any of the foregoing has not occurred, our expected development time and development costs for EFX may be increased.

Even if we were to successfully obtain approval from the FDA and foreign regulatory authorities for EFX, any approval might contain significant limitations related to use, including limitations on the stage of disease EFX is approved to treat, as well as restrictions for specified age groups, warnings, precautions or contraindications. Furthermore, even if we obtain regulatory approval for EFX, we will still need to develop a commercial infrastructure or develop relationships with collaborators to commercialize, establish a commercially viable pricing structure and obtain coverage and adequate reimbursement from third-party payors, including government healthcare programs. If we, or any future collaborators, are unable to successfully commercialize EFX, we may not be able to generate sufficient revenue to continue our business.

We have expended and will continue to expend our limited resources to pursue a particular therapeutic candidate or indication, such as our focus on developing EFX for the treatment of NASH/MASH, and may fail to capitalize on therapeutic candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We have focused our extensive research and development efforts on EFX for the treatment of NASH/MASH. Therefore, we have, and in the future may, forego or delay pursuit of opportunities with other therapeutic candidates or for other indications that later prove to have greater commercial potential. We are highly dependent on the success of the future clinical trials of EFX, the outcomes of which are uncertain. Because EFX is our first and only therapeutic candidate, if it encounters safety, efficacy, supply or manufacturing problems, developmental delays, regulatory or commercialization issues or other problems, the value of our platform could be greatly diminished and our development plans could be curtailed and our business would be significantly harmed.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and EFX for the treatment of NASH/MASH may not yield any commercially viable therapeutic candidates. If we do not accurately evaluate the commercial potential or target market for a particular therapeutic candidate or misread trends in the biopharmaceutical industry, in particular for serious metabolic diseases, we may relinquish valuable rights to that therapeutic candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such therapeutic candidate.

At any time and for any reason, we may determine that one or more of our discovery programs or pre-clinical or clinical therapeutic candidates or programs does not have sufficient potential to warrant the allocation of resources toward such program or therapeutic candidate. Accordingly, we may choose not to develop a potential therapeutic candidate or elect to suspend, deprioritize or terminate one or more of our discovery programs or preclinical or clinical therapeutic candidates or programs. Suspending, deprioritizing or terminating a program or therapeutic candidate in which we have invested significant resources, means we will have expended resources on a program that will not provide a full return on our investment and may have missed the opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or therapeutic candidates.

If we fail to develop and successfully commercialize other product candidates, our business and future prospects may be harmed and our business will be more vulnerable to any problems that we encounter in developing and commercializing our product candidate.

Our product candidate and any future product candidates must undergo rigorous clinical trials and regulatory approvals, and success in nonclinical studies or earlier-stage clinical trials may not be indicative of results in future clinical trials. EFX and any future product candidates will be subject to rigorous and extensive clinical trials and extensive regulatory approval processes implemented by the FDA and similar regulatory bodies in other jurisdictions. The approval process is typically lengthy and expensive, and approval is never certain. As a company, our only experience with clinical trials is our completed BALANCED study, our ongoing HARMONY study, for which we have reported Week 24 results, and our ongoing SYMMETRY study, for which we have reported Week 36 results, and we have not yet completed the clinical trials required to obtain regulatory approval. We may not be able to conduct clinical trials at preferred sites, enlist clinical investigators, enroll sufficient numbers of participants or begin or successfully complete clinical trials in a timely fashion, if at all. Our anticipated clinical trials, including our SYNCHRONY Phase 3 trials, two of which began screening in September 2023, may be insufficient to demonstrate that our potential products will be active, safe or effective. Additional clinical trials may be required if clinical trial results are negative or inconclusive, which will require us to incur additional costs and significant delays.

Success in nonclinical studies and earlier-stage clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the effectiveness and safety of a product candidate. In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to design and execute a clinical trial to support regulatory approval for a NASH/MASH therapy. In addition, there is a high failure rate for drugs and products proceeding through clinical trials. In fact, many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in nonclinical studies and earlier-stage clinical trials. Similarly, the outcome of nonclinical studies may not predict the success of clinical trials. Moreover, data obtained from nonclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product development. Additionally, we are developing a pre-filled, dual-chamber syringe presentation of EFX that is considered to be a biologic-device combination product by the FDA, and any BLA for EFX will require review and coordination by FDA's drug and device centers prior to approval. Any such delays could negatively impact our business, financial condition, results of operations and prospects. From time to time, we may publish interim "top-line" or preliminary data from our clinical trials. Preliminary or interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or interim data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business and financial prospects.

In addition, certain of our hypotheses regarding the potential clinical and therapeutic benefit of EFX compared to other candidates in development for NASH/MASH are based on cross-trial comparisons of results that were not derived from head-to-head preclinical studies or clinical trials. These observations, which do not reflect robust comparative analyses, may suggest misleading similarities or differences due to differences in study protocols, conditions and patient populations, and may not be reliable predictors of the relative efficacy or other benefits of EFX compared to other product candidates that are in development for the treatment of NASH/MASH.

We may develop EFX, and potentially future product candidates, in combination with other therapies, which exposes us to additional risks.

We may develop EFX and future product candidates in combination with one or more approved therapies. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. This could result in our own products being removed from the market or being less successful commercially.

We may also evaluate EFX or any other future product candidates in combination with one or more other therapies that have not yet been approved for marketing by the FDA or similar regulatory authorities outside of the United States. We will not be able to market and sell EFX or any product candidate we develop in combination with any such unapproved therapies that do not ultimately obtain marketing approval. If the FDA or similar regulatory authorities outside of the United States do not approve these other drugs or revoke their approval, or if safety, efficacy, manufacturing, or supply issues arise with the drugs we choose to evaluate in combination with EFX or any other product candidate we develop, we may be unable to obtain approval of or market EFX or any other product candidate we develop.

If we are not successful in discovering, developing, receiving regulatory approval for and commercializing EFX and any future product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.

Although we plan to devote a majority of our resources to the continued nonclinical and clinical testing and potential approval of EFX for the treatment of patients with NASH/MASH, another key element of our strategy is to discover, develop and commercialize a portfolio of products. We are seeking to do so through the identification and potential development of additional pipeline programs, but our resources are limited, and those that we have are geared towards nonclinical and clinical testing and seeking regulatory approval of EFX for the treatment of patients with NASH/MASH. We may also explore strategic collaborations for the development or acquisition of new product candidates, but we may not be successful in entering into such relationships. EFX is our only product candidate in clinical stages of development. Research programs to identify product candidates require substantial technical, financial and human resources, regardless of whether any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- an approved product may not be accepted as safe and effective by trial participants, the medical community or third-party payors; and
- intellectual property or other proprietary rights of third parties for product candidates we develop may potentially block our entry into certain markets or make such entry economically impracticable.

Risks Related to our License and Third-Parties

We may be required to make significant payments under our license agreement for EFX.

We acquired worldwide, exclusive rights to EFX pursuant to our license agreement with Amgen, which we refer to as the Amgen Agreement. Under the Amgen Agreement, in consideration for the license, we made an upfront payment of \$5.0 million to Amgen and also issued 2,653,333 shares of our Series A convertible preferred stock to Amgen at the time of the initial closing of our Series A Preferred Stock financing in June 2018, with a subsequent 3,205,128 shares of our Series A convertible preferred stock issued at the time of the second closing of the Series A Preferred Stock financing in November 2018. On July 2, 2019, we announced the dosing of the first patient in the BALANCED study of EFX, which resulted in a \$2.5 million milestone obligation under the Amgen Agreement. As additional consideration for the license, we are required to pay Amgen \$7.5 million in connection with dosing the first patient in a Phase 3 clinical trial, up to \$30.0 million in connection with marketing approvals and aggregate milestone payments of up to \$75.0 million upon the achievement of specified commercial milestones. Commencing on the first commercial sale of licensed products, we are obligated to pay tiered royalties of low to high single-digit percentages on annual net sales of the products covered by the license. If milestone or other non-royalty obligations become due, we may not have sufficient funds available to meet our obligations, which will materially adversely affect our business operations and financial condition.

If we breach our license agreement with Amgen related to EFX, we could lose the ability to continue the development and commercialization of EFX.

We are dependent on patents, know-how and proprietary technology in-licensed from Amgen. Our commercial success depends upon our ability to develop, manufacture, market and sell our product candidate or any future product candidates and use our and our licensor's proprietary technologies without infringing the proprietary rights of third parties. Amgen may have the right to terminate the license agreement in full in the event we materially breach or default in the performance of any of the obligations under the license agreement. A termination of the license agreement with Amgen could result in the loss of significant rights and could harm our ability to commercialize our product candidates.

Disputes may also arise between us and Amgen, as well as any future potential licensors, regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidate and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

In addition, the Amgen Agreement under which we currently license intellectual property is complex, and certain provisions may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property, or increase what we believe to be our financial or other obligations under the Amgen Agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangement on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described below. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer.

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

We may pursue collaborations in order to develop and commercialize EFX and any future product candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products and the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborators may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we may not be able to further develop our product candidate or any future product candidates or bring them to market and generate product revenue.

Risks Related to Employee Matters and Growth

We must attract and retain highly skilled employees in order to succeed. If we are not able to retain our current senior management team and our scientific advisors or continue to attract and retain qualified scientific, technical and business personnel, our business will suffer.

To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel and we face significant competition for experienced personnel. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. We are dependent on the members of our management team and our scientific advisors for our business success. We do not maintain “key person” insurance for any of our key personnel. An important element of our strategy is to take advantage of the research and development expertise of our current management and to utilize the expertise of our scientific advisors in the NASH/MASH field. We currently have employment agreements with all of our executive officers. Our employment agreements with our executive officers are terminable by them without notice and some provide for severance and change in control benefits. The loss of any one of our executive officers or key scientific consultants could result in a significant loss in the knowledge and experience that we, as an organization, possess and could cause significant delays, or outright failure, in the development and further commercialization of our product candidate or any future product candidates.

There is intense competition for qualified personnel, including management, in the technical fields in which we operate, and we may not be able to attract and retain qualified personnel necessary for the successful research, development and commercialization of EFX or any future product candidates. In particular, we have experienced a very competitive hiring environment in the San Francisco Bay Area, where we are headquartered. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success with which we can discover and develop product candidates and our business will be limited.

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We cannot ensure that our compliance controls, policies, and procedures will in every instance protect us from acts committed by our employees, agents, contractors, or collaborators that would violate the law or regulation, including, without limitation, healthcare, employment, foreign corrupt practices, environmental, competition, and patient privacy and other privacy laws and regulations. Such improper actions could subject us to civil or criminal investigations, and monetary and injunctive penalties, and could adversely impact our ability to conduct business, operating results, and reputation.

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to comply with the laws enforced by the FDA and other similar foreign regulatory bodies, fails to provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies, fails to comply with manufacturing standards we have established, fails to comply with healthcare fraud and abuse laws in the United States and similar foreign laws, or fails to report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under these laws will increase significantly, and our costs associated with compliance with these laws are also likely to increase. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of 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, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations.

We may encounter difficulties in managing our growth, which could adversely affect our operations.

As of October 31, 2023, we had 51 full-time employees and one part-time employee. As we continue development and pursue the potential commercialization of EFX and other product candidates, as well as function as a public company, we will need to expand our financial, development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, suppliers and other third parties. Our future financial performance and our ability to develop and commercialize our product candidate and to compete effectively will depend, in part, on our ability to manage any future growth effectively.

We may acquire additional technology and complementary businesses in the future. Acquisitions involve many risks, any of which could materially harm our business, including the diversion of management's attention from core business concerns, failure to effectively exploit acquired technologies, failure to successfully integrate the acquired business or realize expected synergies or the loss of key employees from either our business or the acquired businesses.

Our success depends upon our ability to obtain and maintain intellectual property protection for our products and technologies. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.

Our success will depend in significant part on our and our current or future licensors', licensees' or collaborators' ability to establish and maintain adequate protection of our intellectual property covering the product candidates we plan to develop, and the ability to develop these product candidates and commercialize the products resulting therefrom, without infringing the intellectual property rights of others. We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our products and compositions, their methods of use, and any other inventions that are important to the development of our business. In addition to taking other steps to protect our intellectual property, we have applied for, and intend to continue to apply for, patents with claims covering our technologies, processes and product candidates when and where we deem it appropriate to do so. Our in-licensed patents and patent applications in both United States and certain foreign jurisdictions relate to EFX and related Fc-fusion polypeptides. There can be no assurance that the claims of our patents or any patent application that issues as a patent, will exclude others from making, using or selling our product candidate or any future product candidates or products that are substantially similar to our product candidate or any future product candidates. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. In countries where we have not and do not seek patent protection, third parties may be able to manufacture and sell our product candidate or any future product candidates without our permission, and we may not be able to stop them from doing so.

With respect to patent rights, we do not know whether any of the pending patent applications for our product candidate or any future product candidates will result in the issuance of patents that effectively protect our technologies, processes and product candidates, or if any of our issued patents or our current or future licensors', licensees' or collaborators' issued patents will effectively prevent others from commercializing competitive technologies, processes and products. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or in some cases not at all, until they are issued as a patent. Therefore, we cannot be certain that we or our current or future licensors, licensees or collaborators were the first to make or file on the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our current or future licensors, licensees or collaborators were the first to file for patent protection of such inventions. There is also no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which could be used by a third party to challenge the validity of our patents, should they issue, or prevent a patent from issuing from a pending patent application. Any of the foregoing could harm our competitive position, business, financial condition, results of operations, and prospects.

Any changes we make to our product candidate or any future product candidates, including formulations that may be required for commercialization, or that cause them to have what we view as more advantageous properties may not be covered by our existing patents and patent applications, and we may be required to file new applications and/or seek other forms of protection for any such altered product candidates. The patent landscape surrounding the technology underlying our product candidate or any future product candidates is crowded, and there can be no assurance that we would be able to secure patent protection that would adequately cover an alternative to our product candidate or any future product candidates.

The patent prosecution process is expensive and time-consuming, and we and our current or future licensors, licensees or collaborators may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our current or future licensors, licensees or collaborators will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection for them. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering technology that we license from or license to third parties and may be reliant on our current or future licensors, licensees or collaborators to perform these activities, which means that these patent applications may not be prosecuted, and these patents enforced, in a manner consistent with the best interests of our business. If our current or future licensors, licensees or collaborators fail to establish, maintain, protect or enforce such patents and other intellectual property rights, such rights may be reduced or eliminated. If our current or future licensors, licensees or collaborators are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised.

The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, which in recent years have been the subject of much litigation, and, therefore, the issuance, scope, validity, enforceability, and commercial value of any patent claims that we have rights or may obtain cannot be predicted with certainty. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. As a result, the issuance, scope, validity, enforceability and commercial value of our and our current or future licensors', licensees' or collaborators' patent rights are highly uncertain. Our and our current or future licensors', licensees' or collaborators' pending and future patent applications may not result in patents being issued that protect our technology or product candidates, or products resulting therefrom, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. The patent examination process may require us or our current or future licensors, licensees or collaborators to narrow the scope of the claims of pending and future patent applications, which would limit the scope of patent protection that is obtained, if any. Our and our current or future licensors', licensees' or collaborators' patent applications cannot be enforced against third parties practicing the technology that is currently claimed in such applications unless and until a patent issues from such applications, and then only to the extent the claims that issue are broad enough to cover the technology being practiced by third parties.

Furthermore, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after the resulting products are commercialized. As a result, our owned and in-licensed patents may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. We expect to seek extensions of patent terms for our issued patents, where available. This includes in the United States under the Hatch-Waxman Act, which permits a patent term extension of up to five years beyond the original expiration date of the patent as compensation for regulatory delays. However, such a patent term extension cannot lengthen the remaining term of a patent beyond a total of 14 years from the product's approval date. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent and within 60 days of product approval. During the period of patent term extension, the claims of a patent are not enforceable for their full scope but are instead limited to the scope of the approved product. In addition, the applicable authorities, including the FDA in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. In addition, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to the expiration of relevant patents or otherwise failing to satisfy applicable requirements. If this occurs, any period during which we have the right to exclusively market our product will be shorter than we would otherwise expect, and our competitors may obtain approval of and launch products earlier than might otherwise be the case.

Patent terms may be inadequate to protect our competitive position on our product candidate or any future product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. A number of U.S. patents directed to various aspects of EFX will expire in 2029; we currently anticipate that a composition of matter patent will be eligible for patent term extension to 2034. Even if patents covering our product candidate or any future product candidate are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our product candidate or any future product candidate might expire before or shortly after we or our partners commercialize those candidates. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

The legal protection afforded to inventors and owners of intellectual property in countries outside of the United States may not be as protective or effective as that in the United States and we may, therefore, be unable to acquire and enforce intellectual property rights outside the United States to the same extent as in the United States. Whether filed in the United States or abroad, our patent applications may be challenged or may fail to result in issued patents.

In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing or commercializing competing products. Furthermore, others may independently develop or commercialize similar or alternative technologies or drugs, or design around our patents. Our patents may be challenged, invalidated, circumvented or narrowed, or fail to provide us with any competitive advantages. In many foreign countries, patent applications and/or issued patents, or parts thereof, must be translated into the native language. If our patent applications or issued patents are translated incorrectly, they may not adequately cover our technologies; in some countries, it may not be possible to rectify an incorrect translation, which may result in patent protection that does not adequately cover our technologies in those countries.

Filing, prosecuting, enforcing and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States are less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and certain state laws in the United States. Consequently, we and our licensor may not be able to prevent third parties from practicing our and our licensor's inventions in all countries outside the United States, or from selling or importing products made using our and our licensor's inventions in and into the United States or other jurisdictions. Competitors may use our and our licensor's technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we and our licensor have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidate or any future product candidates and our and our licensor's 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 foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biotechnology. This could make it difficult for us and our licensor to stop the infringement of our and our licensor's patents or the marketing of competing products in violation of our and our licensor's proprietary rights, generally. Proceedings to enforce our and our licensor's patent rights in foreign jurisdictions could result in substantial costs and divert our and our licensor's efforts and attention from other aspects of our business, could put our and our licensor's patents at risk of being invalidated or interpreted narrowly, could place our and our licensor's patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensor. We or our licensor may not prevail in any lawsuits that we or our licensor initiate and the damages or other remedies awarded, if any, may not be commercially meaningful.

The requirements for patentability differ in certain countries, particularly developing countries. For example, China has a heightened requirement for patentability and, specifically, requires a detailed description of medical uses of a claimed drug. In addition, India, certain countries in Europe and certain developing countries, including Thailand, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensor may have limited remedies if patents are infringed or if we or our licensor are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. Accordingly, our and our licensor's efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

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

Periodic maintenance and annuity fees on issued United States patents and most foreign patent applications and patents must be paid to the U.S. Patent and Trademark Office ("USPTO") and foreign patent agencies, respectively, in order to maintain such patents and patent applications. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application, examination and issuance processes. While an inadvertent lapse can, in some cases, be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensor fail to maintain the patents and patent applications covering our product candidate or any future product candidates, our competitors might be able to enter the market with similar or identical products or technology, which would have a material adverse effect on our business, financial condition and results of operations.

We may be unable to obtain intellectual property rights or technology necessary to develop and commercialize EFX or any future product candidates.

Several third parties are actively researching and seeking and obtaining patent protection in the NASH/MASH field, and there are issued third-party patents and published third-party patent applications in these fields. However, we may not be aware of all third-party intellectual property rights potentially relating to our product candidate or any future product candidates and technologies.

Depending on what patent claims ultimately issue and how courts construe the issued patent claims, as well as depending on the ultimate formulation and method of use of our product candidate or any future product candidates, we may need to obtain a license under such patents. There can be no assurance that such licenses will be available on commercially reasonable terms, or at all. If a third party does not offer us a necessary license or offers a license only on terms that are unattractive or unacceptable to us, we might be unable to develop and commercialize one or more of our product candidate or any future product candidates, which would have a material adverse effect on our business, financial condition and results of operations. Moreover, even if we obtain licenses to such intellectual property, but subsequently fail to meet our obligations under our license agreements, or such license agreements are terminated for any other reasons, we may lose our rights to in-licensed technologies.

The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment, or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Our inability to protect our confidential information and trade secrets would harm our business and competitive position.

In addition to seeking patents for some of our technology and products, in our activities we also rely substantially on trade secrets, including unpatented know-how, technology and other proprietary materials and information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, these steps may be inadequate, we may fail to enter into agreements with all such parties or any of these parties may breach the agreements and disclose our proprietary information and there may be no adequate remedy available for such breach of an agreement. We cannot assure you that our proprietary information will not be disclosed or that we can meaningfully protect our trade secrets. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts both within and outside the United States may be less willing, or unwilling, to protect trade secrets. If a competitor lawfully obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

We may become involved in lawsuits or other proceedings to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful and have a material adverse effect on the success of our business.

Third parties may infringe our or our licensor's patents or misappropriate or otherwise violate our or our licensor's intellectual property rights. In the future, we or our licensor may initiate legal proceedings to enforce or defend our or our licensor's intellectual property rights, to protect our or our licensor's trade secrets or to determine the validity or scope of intellectual property rights we own or control. Also, third parties may initiate legal proceedings against us or our licensor to challenge the validity or scope of intellectual property rights we own, control or to which we have rights. For example, generic or biosimilar drug manufacturers or other competitors or third parties may challenge the scope, validity or enforceability of our or our licensor's patents, requiring us or our licensor to engage in complex, lengthy and costly litigation or other proceedings. These proceedings can be expensive and time-consuming and many of our or our licensor's adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. Moreover, the outcome following legal assertions of invalidity and unenforceability is unpredictable. Accordingly, despite our or our licensor's efforts, we or our licensor may not be able to prevent third parties from infringing upon or misappropriating intellectual property rights we own, control or have rights to, particularly in countries where the laws may not protect those rights as fully as in the United States. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, if we or our licensor initiated legal proceedings against a third party to enforce a patent covering a product candidate, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. In an infringement or declaratory judgment proceeding, a court may decide that a patent owned by or licensed to us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our or our licensor's patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our or our licensor's patents at risk of being invalidated, narrowed, held unenforceable or interpreted in such a manner that would not preclude third parties from entering the market with competing products.

Third-party pre-issuance submission of prior art to the USPTO, or opposition, derivation, revocation, reexamination, *inter partes* review or interference proceedings, or other pre-issuance or post-grant proceedings or other patent office proceedings or litigation in the United States or other jurisdictions provoked by third parties or brought by us or our licensor, may be necessary to determine the inventorship, priority, patentability or validity of inventions with respect to our or our licensor's patents or patent applications. An unfavorable outcome could leave our technology or product candidates without patent protection, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or could require us or our licensor to obtain license rights from the prevailing party in order to be able to manufacture or commercialize our product candidate or any future product candidates without infringing third-party patent rights. Our business could be harmed if the prevailing party does not offer us or our licensor a license on commercially reasonable terms, or at all. Even if we or our licensor obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensor. In addition, if the breadth or strength of protection provided by our or our licensor's patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or any future product candidates. Even if we successfully defend such litigation or proceeding, we may incur substantial costs and it may distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into collaborations.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, many foreign jurisdictions have rules of discovery that are different than those in the United States and which may make defending or enforcing our or our licensor's patents extremely difficult. There could also 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 material adverse effect on the price of shares of our common stock.

Third parties may initiate legal proceedings against us alleging that we infringe their intellectual property rights or we may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell any product candidates that we may develop and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Third parties may initiate legal proceedings against us or our licensor alleging that we or our licensor infringe their intellectual property rights or we or our licensor may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, including in oppositions, interferences, revocations, reexaminations, *inter partes* review or derivation proceedings before the USPTO or its counterparts in other jurisdictions. These proceedings can be expensive and time-consuming and many of our or our licensor's adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensor can.

An unfavorable outcome in any such proceeding could require us or our licensor to cease using the related technology or developing or commercializing our product candidate or any future product candidates, or to attempt to license rights to it from the prevailing party, which may not be available on commercially reasonable terms, or at all.

We could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidate or any future product candidates or force us to cease some of our business operations, which could materially harm our business.

We perform searches of patent and scientific databases in order to identify documents that may be of potential relevance to the freedom-to-operate and/or patentability of our product candidate or any future product candidates. In general, such searches are conducted based on keywords, sequences, inventors/authors and assignees/entities to capture U.S. and European patents and patent applications, PCT publications and scientific journal articles.

The patent landscape around our EFX product candidate is complex, and we may not be aware of all third-party intellectual property rights potentially relating to our product candidate or any future product candidates and technologies. Moreover, it is possible that we are or may become aware of patents or pending patent applications that we think do not relate to our product candidate or any future product candidates or that we believe are invalid or unenforceable, but that may nevertheless be interpreted to encompass our product candidate or any future product candidates and to be valid and enforceable. As to pending third-party applications, we cannot predict with any certainty which claims will issue, if any, or the scope of such issued claims. If any third-party intellectual property claims are asserted against us, even if we believe the claims are without merit, there is no assurance that a court would find in our favor, e.g., on questions of infringement, validity, enforceability or priority. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could materially and adversely affect our ability and the ability of our licensor to commercialize any product candidates we may develop, and any other product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If any such third-party patents (including those that may issue from such applications) were successfully asserted against us or our licensor or other commercialization partners and we were unable to successfully challenge the validity or enforceability of any such asserted patents, then we or our licensor and other commercialization partners may be prevented from commercializing our product candidate or any future product candidates, or may be required to pay significant damages, including treble damages and attorneys' fees if we are found to willfully infringe the asserted patents, or obtain a license to such patents, which may not be available on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. 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. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. Any of the foregoing would have a material adverse effect on our business, financial condition and operating results.

We may be subject to claims by third parties asserting that our employees or we have misappropriated a third party's intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, including our senior management, were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. We may be subject to claims that we or these employees have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such employee's former employer, or that third parties have an interest in our patents as an inventor or co-inventor. Litigation may be necessary to defend against these claims. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain other damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms, or at all. Even if we successfully prosecute or defend against such claims, litigation could result in substantial costs and distract management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations and prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to any product candidates we may develop or utilize similar technology but that are not covered by the claims of the patents that we license or may own in the future;
- we, or our current or future collaborators, might not have been the first to make the inventions covered by the issued patents and pending patent applications that we license or may own in the future;
- we, or our current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO.

If we or our licensing partner initiate legal proceedings against a third party to enforce a patent covering our product candidate or any future product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These types of mechanisms include *inter partes* review, post grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). These types of proceedings could result in revocation or amendment to our patents such that they no longer cover our product candidates. The outcome for any particular patent following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. A loss of patent protection for our product candidates could have a material adverse impact on our ability to commercialize or license our technology and product candidates and, resultantly, on our business, financial condition, prospects and results of operations.

Likewise, patents directed to our proprietary technologies and our product candidates may expire before or soon after our first product achieves marketing approval in the United States or foreign jurisdictions. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on our business, financial condition, prospects and results of operations. A number of U.S. patents directed to various aspects of EFX will expire in 2029; we currently anticipate that a composition of matter patent will be eligible for patent term extension to 2034.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidate or any future product candidates.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves technological and legal complexity, and obtaining and enforcing biotechnology patents is costly, time-consuming and inherently uncertain. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances, weakening the rights of patent owners in certain situations or ruling that certain subject matter is not eligible for patent protection. In addition to increasing uncertainty with regard to our and our licensor's ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts, the USPTO and equivalent bodies in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our and our licensor's ability to obtain new patents or to enforce existing patents and patents we and our licensor may obtain in the future.

Patent reform laws, such as the Leahy-Smith America Invents Act ("the Leahy-Smith Act") as well as changes in how patent laws are interpreted, could increase the uncertainties and costs surrounding the prosecution of our and our licensor's patent applications and the enforcement or defense of our or our licensor's issued patents, all of which could have a material adverse effect on our business, financial condition and results of operations.

Risks Related to Government Regulation

Risks Related to Obtaining Regulatory Approval

We have limited experience in conducting clinical trials and have never obtained approval for any product candidates, and may be unable to do so successfully.

As a company, other than the completed BALANCED study and our ongoing HARMONY and SYMMETRY studies, we have no experience in designing, conducting or completing clinical trials and have never progressed a product candidate through to regulatory approval. In part because of this lack of experience, our clinical trials may require more time and incur greater costs than we anticipate. We cannot be certain that our planned clinical trials, including the SYNCHRONY Phase 3 trials, will begin or conclude on time, if at all. Large-scale trials will require significant additional financial and management resources. Any performance failure on the part of such third parties could delay the clinical development of our product candidate or any future product candidates or delay or prevent us from obtaining regulatory approval or commercializing our current or any future product candidates, depriving us of potential product revenue and resulting in additional losses.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. Our inability to obtain regulatory approval for EFX or any future product candidate would substantially harm our business.

The time required to obtain approval from the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of nonclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's development and may vary among jurisdictions.

EFX or our future product candidates could fail to receive regulatory approval from the FDA or a comparable foreign regulatory authority for many reasons, including:

- disagreement with the design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective for its proposed indication;
- failure of clinical trials to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- disagreement with our interpretation of data from nonclinical studies or clinical trials;

- the insufficiency of data collected from clinical trials of EFX or any future product candidates to obtain regulatory approval;
- failure to obtain approval of the manufacturing processes or facilities of third-party manufacturers with whom we contract for clinical and commercial supplies; or
- changes in the approval policies or regulations that render our nonclinical and clinical data insufficient for approval.

The FDA or a comparable foreign regulatory authority may require more information, including additional nonclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program for other reasons. If we were to obtain approval, regulatory authorities may approve EFX or any future product candidates for fewer or more limited indications than we request, may require labeling or a Risk Evaluation and Mitigation Strategy ("REMS") that includes significant use or distribution restrictions or safety warnings, precautions, or contraindications, may grant approval contingent on the performance of costly post-marketing clinical trials or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate.

Additional time may be required to obtain regulatory approval for our product candidates because they are combination products.

EFX is being developed, and future product candidates may be developed, as combination products that require coordination within the FDA and similar foreign regulatory agencies for review of their device and drug/biologic components. Medical products containing a combination of new drugs, biological products or medical devices may be regulated as "combination products" in the United States and Europe. A combination product generally is defined as a product comprised of components from two or more regulatory categories (e.g., drug/device, device/biologic, drug/biologic). Each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a new drug, biologic or device. In order to facilitate pre-market review of combination products, the FDA designates one of its centers to have primary jurisdiction for the pre-market review and regulation of the overall product based upon a determination by the FDA of the primary mode of action of the combination product. Where approval of the drug or biologic and device is sought under a single application, there could be delays in the approval process due to the increased complexity of the review process and the lack of a well-established review process and criteria. The EMA has a parallel review process in place for combination products, the potential effects of which in terms of approval and timing could independently affect our ability to market our combination products in Europe.

While we intend to seek designations for our product candidates with the FDA and comparable other regulatory authorities that are intended to confer benefits such as a faster development process or an accelerated regulatory pathway, there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.

The FDA and comparable other regulatory authorities offer certain designations for product candidates that are designed to encourage the research and development of product candidates that are intended to address conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities, a potentially accelerated regulatory pathway and priority review. Despite these designations, there can be no assurance that we will successfully obtain these or other designations for any of our other product candidates. In addition, while such designations could expedite the development or review process, they generally do not change the standards for approval. Even if we obtain such designations for one or more of our product candidates, there can be no assurance that we will realize their intended benefits.

For example, we have received a Breakthrough Therapy designation for EFX for the treatment of NASH/MASH and we may seek a Breakthrough Therapy designation for some of our product candidates in the future. A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in control regimens. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for designation.

In addition, in October 2021, the FDA granted Fast Track designation for EFX for the treatment of NASH/MASH, and we may seek Fast Track Designation for some of our future product candidates. If a therapy is intended for the treatment of a serious or life-threatening condition and the therapy demonstrates the potential to address unmet medical needs for this condition, the therapy sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track Designation, as we have for EFX for the treatment of NASH/MASH, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track Designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

Biologics designated as breakthrough therapies or granted Fast Track designation by the FDA may also be eligible for other expedited approval programs, including accelerated approval. A product candidate may be eligible for accelerated approval if it treats a serious or life-threatening condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. As a condition of accelerated approval, the FDA may require that a sponsor of a product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence. Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product granted accelerated approval. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. In addition, FDORA gives the FDA increased authority to withdraw accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit. The FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. Accelerated approval may also be withdrawn if, among other things, a confirmatory trial required to verify the predicted clinical benefit of the product fails to verify such benefit or if such trial is not conducted with due diligence. In addition, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Thus, even if we seek to utilize the accelerated approval pathway, we may not be able to obtain accelerated approval and, even if we do, we may not experience a faster development, regulatory review or approval process for that product. In addition, receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a traditional approval.

We may seek priority review designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster regulatory review or approval process.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not result in expedited development and does not necessarily result in expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

Our failure to obtain regulatory approval in international jurisdictions would prevent us from marketing EFX or any future product candidates outside the United States.

We intend to market any approved products in the United States, the EU, Japan and other foreign jurisdictions. Even if our products are approved for marketing in the United States, in order to market and sell our products in other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, we must secure product reimbursement approvals before regulatory authorities will approve the product for sale in that country. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country. For example, even if EFX is approved in the United States, the EMA may require more information, including additional nonclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans in the EU. Moreover, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others.

Also, regulatory approval for our product candidate or any future product candidates may be withdrawn if we fail to comply with regulatory requirements, if problems occur after the product candidate reaches the market or for other reasons. If we fail to comply with the regulatory requirements in international markets and fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidate or any future product candidates will be harmed and our business will be adversely affected. We may not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions. 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. If we fail to obtain approval of our product candidate or any future product candidates by regulatory authorities in another country, we will be unable to commercialize our product in that country, and the commercial prospects of that product candidate and our business prospects could decline.

Even if we are able to obtain regulatory approvals for our product candidate or any future product candidates, if they exhibit harmful side effects after approval, our regulatory approvals could be revoked or otherwise negatively impacted, and we could be subject to costly and damaging product liability claims.

Clinical trials are conducted in representative samples of the potential patient population which may have significant variability. Even if we receive regulatory approval for EFX or any of our future product candidates, we will have tested them in only a small number of patients during our clinical trials. Clinical trials are by design based on a limited number of subjects and of limited duration for exposure to the product used to determine whether, on a potentially statistically significant basis, the planned safety and efficacy of any product candidate can be achieved. As with the results of any statistical sampling, we cannot be sure that all side effects of our product candidates may be uncovered, and it may be the case that only with a significantly larger number of patients exposed to the product candidate for a longer duration, may a more complete safety profile be identified. Further, even larger clinical trials may not identify rare serious adverse effects or the duration of such studies may not be sufficient to identify when those events may occur. If our applications for marketing are approved and more patients begin to use our product, new risks and side effects associated with our products may be discovered. There have been other products that have been approved by the regulatory authorities but for which safety concerns have been uncovered following approval. Such safety concerns have led to labelling changes or withdrawal of products from the market, and any of our product candidates may be subject to similar risks. Additionally, we may be required to conduct additional nonclinical and clinical trials, require additional warnings on the label of our product candidate, reformulate our product or make changes, create a medication guide outlining the risks of such side effects for distribution to patients and obtain new approvals for our and our suppliers' manufacturing facilities for EFX and any future product candidates. We might have to withdraw or recall our products from the marketplace. We may also experience a significant drop in the potential sales of our product if and when regulatory approvals for such product are obtained, experience harm to our reputation in the marketplace or become subject to lawsuits, including class actions. Any of these results could decrease or prevent any sales of our approved product or substantially increase the costs and expenses of commercializing and marketing our product.

Even if our current product candidate or any future product candidates receive regulatory approval, they will remain subject to extensive regulatory scrutiny and may still face future development and regulatory difficulties.

Even if we obtained regulatory approval for a product candidate, regulatory authorities may still impose significant restrictions on our product candidates, including their indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies. For example, if EFX is approved by the FDA based on a surrogate endpoint pursuant to accelerated approval regulations (also referred to as Subpart E regulations), we will be required to conduct additional confirmatory clinical trials demonstrating the clinical benefit on the ultimate outcome of NASH/MASH. Further, even if we obtained regulatory approval for a product candidate, it would be subject to ongoing requirements by the FDA and comparable foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information.

The FDA and comparable foreign regulatory authorities will continue to closely monitor the safety profile of any product even after approval. If the FDA or comparable foreign regulatory authorities become aware of new safety information after approval of our product candidate or any future product candidates, they may require labeling changes or establishment of a risk evaluation and mitigation strategy or similar strategy, impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance.

In addition, manufacturers of our products, if approved, and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP and applicable QSRs, regulations and standards. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we, EFX, or any future product candidates or the manufacturing facilities for EFX, the delivery device used for EFX, or any future product candidates fail to comply with applicable regulatory requirements, or undesirable side effects caused by such products are identified, a regulatory agency may:

- issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings about such product;
- mandate modifications to instructions for use;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require that we conduct post-marketing studies;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend marketing of, withdraw regulatory approval of or recall such product;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products or require us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product and generate revenue.

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the Department of Justice, the Department of Health and Human Services' Office of Inspector General, state attorneys general, members of Congress and the public. Violations, including promotion of our products for unapproved (or off-label) uses, are subject to enforcement letters, inquiries and investigations, and civil and criminal sanctions by the government. Additionally, comparable foreign regulatory authorities will heavily scrutinize advertising and promotion of any product candidate that obtains approval outside of the United States.

In the United States, engaging in the impermissible promotion of our products for off-label uses can also subject us to false claims litigation under federal and state statutes, which can lead to civil and criminal penalties and fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. These false claims statutes include the federal False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government prevails in the lawsuit, the individual will share in any fines or settlement funds. Since 2004, these federal False Claims Act lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements regarding certain sales practices promoting off-label drug uses involving fines in excess of \$1 billion. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations and be excluded from Medicare, Medicaid and other federal and state healthcare programs. If we do not lawfully promote our approved products, we may become subject to such litigation and, if we do not successfully defend against such actions, those actions may have a material adverse effect on our business, financial condition and results of operations.

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

Risks Related to Healthcare Regulation

The advancement of healthcare reform may negatively impact our ability to profitably sell our product candidate or any future product candidates, if approved.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidate or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the Affordable Care Act or ACA, was enacted, which includes measures that have significantly changed the way health care is financed by both governmental and private insurers. Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an Executive Order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The Executive Order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administrations or other efforts, if any, to challenge repeal or replace the ACA, will impact our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. The U.S. Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction, which triggered the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of, on average, 2% per fiscal year through 2031 unless Congress takes additional action. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. CMS has published a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government reimbursement methodologies for drugs.

In addition, President Biden has issued multiple executive orders that have sought to reduce prescription drug costs. In February 2023, HHS also issued a proposal in response to an October 2022 executive order issued by President Biden that includes a proposed prescription drug pricing model that will test whether targeted Medicare payment adjustments will sufficiently incentivize manufacturers to complete confirmatory trials for drugs approved through FDA's accelerated approval pathway. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden Administration may reverse or otherwise change these measures, both the Biden Administration and the U.S. Congress have indicated that they will continue to seek new legislative measures to control drug costs.

In August 2022, the Inflation Reduction Act of 2022 (the "IRA") was signed into law. The IRA includes several provisions that will impact our business to varying degrees, including provisions that reduce the out-of-pocket spending cap for Medicare Part D beneficiaries from \$7,050 to \$2,000 starting in 2025, thereby effectively eliminating the coverage gap, allow the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay until January 1, 2032 the implementation of the HHS rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, if they have one rare disease designation and the only approved indication is for that rare disease. If a product receives multiple rare disease designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The effect of IRA on our business and the healthcare industry in general is not yet known.

We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our approved products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability. Although a number of these, and other proposed measures may require additional authorization to become effective, and the Biden administration may reverse or otherwise change these measures, Congress has indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private third-party payors.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. 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. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations, which, if violated, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare providers, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, and if approved, market, sell and distribute our products. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits persons from, among other things, 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, the referral of an individual for the furnishing or arranging for the furnishing, or the purchase, lease or order, or arranging for or recommending purchase, lease or order, of any good or service for which payment may be made under a federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which can be enforced through civil whistleblower or *qui tam* actions, prohibit individuals or entities from, among other things knowingly presenting, or causing to be presented, to the federal government or a government contractor, grantee, or other recipient of federal funds, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government; knowingly making, using or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The federal False Claims Act also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery;
- the federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) imposes criminal liability for knowingly and willfully executing a scheme to defraud any healthcare benefit program, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense or knowingly and willfully making false statements relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”) and their implementing regulations, including the Final Omnibus Rule published in January 2013, imposes obligations on certain healthcare providers, health plans and healthcare clearinghouses, known as covered entities, as well as their business associates, which are individuals and entities that perform certain services involving the creation, maintenance, receipt, use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;

- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the federal Open Payments program, created under Section 6002 of the Affordable Care Act and its implementing regulations, requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) to report annually to CMS information related to “payments or other transfers of value” made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians (as defined above) and their immediate family members. As of January 1, 2022, these reporting obligations have now extended to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners; and
- analogous state, local, and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug prices; state and local laws that require the registration of pharmaceutical sales representatives; several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales representatives. State and foreign laws, including for example the EU General Data Protection Regulation, which became effective May 2018 also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and state and foreign laws that govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting 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, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and any potential collaborators may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act and California Consumer Privacy Act of 2018 (“CCPA”)), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. The CCPA has been characterized as the first “GDPR-like” privacy statute to be enacted in the United States because it mirrors a number of the key provisions of the EU General Data Protection Regulation (“GDPR”) (discussed below in the European Data Collection subsection). Specifically, the act established a comprehensive privacy framework for covered businesses by creating an expanded definition of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA, as amended by HITECH. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact some of our business activities.

Further, the CCPA was amended by the California Privacy Rights Act (“CPRA”) which entered into force on January 1, 2023. The CPRA creates additional obligations with respect to processing and storing personal information. Additionally, some observers have noted that the CCPA and CPRA could mark the beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business. Already, in the United States, we have witnessed significant developments at the state level with twelve other states passing comprehensive privacy laws that incorporate many similar concepts of the CCPA. Despite the similarities, there are also several key differences in the scope, application, and enforcement of the law that will change the operational practices of regulated businesses. The new laws will, among other things, impact how regulated businesses collect and process personal sensitive data, conduct data protection assessments, transfer personal data to affiliates, and respond to consumer rights requests.

A number of other states have proposed new privacy laws, some of which are similar to the above discussed recently passed laws. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

Compliance with U.S. and international data protection laws and regulations, including the EU GDPR/UK GDPR and other EU and UK data protection laws could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals’ privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

In the event we decide to conduct clinical trials or continue to enroll subjects in our ongoing or future clinical trials, we may be subject to additional privacy restrictions. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the European Economic Area (“EEA”), including personal health data, is subject to the EU General Data Protection Regulation (“EU GDPR”), and similarly, processing of personal data regarding individuals in the UK is subject to the UK General Data Protection Regulation and the UK Data Protection Act 2018 (“UK GDPR” and together with the EU GDPR, “GDPR”). The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA/UK, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million (£17.5 million under UK GDPR) or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers of personal data to countries outside the EEA/UK that are not considered by the European Commission and UK government as providing “adequate” protection to personal data (“third countries”), including the United States. The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities.

To enable the transfer of personal data outside of the EEA or the UK, adequate safeguards (for example, the European Commission approved Standard Contractual Clauses (“SCCs”)) must be implemented in compliance with European and UK data protection laws. In addition, transfers made pursuant to the SCCs (and other similar appropriate transfer safeguards) need to be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular regarding applicable surveillance laws and relevant rights of individuals with respect to the transferred personal data, to ensure an “essentially equivalent” level of protection to that guaranteed in the EEA in the jurisdiction where the data imported is based (“Transfer Impact Assessment”). On June 4, 2021, the EC issued new forms of standard contractual clauses for data transfers from controllers or processors in the EU/EEA (or otherwise subject to the GDPR) to controllers or processors established outside the EU/EEA. The new standard contractual clauses replace the standard contractual clauses that were adopted previously under the EU Data Protection Directive. The UK is not subject to the EC’s new standard contractual clauses but has published its own transfer mechanism, the International Data Transfer Agreement and International Data Transfer Addendum (“IDTA”), a which will enable transfers from the UK, and has also implemented a similar Transfer Impact Assessment requirement. We will be required to implement these new safeguards and carry out Transfer Impact Assessments when conducting restricted data transfers under the GDPR and doing so will require significant effort and cost, and may result in us needing to make strategic considerations around where EEA or UK personal data is stored and transferred, and which service providers we can utilize for the processing of EEA/UK personal data.

Although the UK is regarded as a third country under the EU GDPR, the European Commission has issued a decision recognizing the UK as providing adequate protection under the EU GDPR (“Adequacy Decision”) and, therefore, transfers of personal data originating in the EEA to the UK remain unrestricted. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The UK Government has also now introduced a Data Protection and Digital Information Bill (“UK Bill”) into the UK legislative process. The aim of the UK Bill is to reform the UK’s data protection regime following Brexit. If passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EEA data protection regime and threaten the UK Adequacy Decision from the EU Commission. This may lead to additional compliance costs and could increase our overall risk. The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties.

Compliance with the above and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, financial condition and results of operations.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenue, if any.

In some countries, particularly the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. 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. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our drug candidate to other available procedures. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Healthcare insurance coverage and reimbursement may be limited or unavailable for our product candidate, if approved, which could make it difficult for us to sell our product candidate or other therapies profitably.

The success of our product candidate, if approved, depends on the availability of coverage and adequate reimbursement from third-party payors including governmental healthcare programs, such as Medicare and Medicaid, commercial payors, and health maintenance organizations. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Coverage and adequate reimbursement from third-party payors are critical to new product acceptance.

Third-party payors decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a product from a third-party payor is a time consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS, an agency within HHS, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private third-party payors tend to follow Medicare coverage and reimbursement limitations to a substantial degree, but also have their own methods and approval process apart from Medicare determinations. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement.

In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price ("ASP") and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

Our activities in the United States subject us to various laws relating to foreign investment and the export of certain technologies, and our failure to comply with these laws or adequately monitor the compliance of our suppliers and others we do business with could subject us to substantial fines, penalties and even injunctions, the imposition of which on us could have a material adverse effect on the success of our business.

Because we have substantial operations in the United States, we are subject to U.S. laws that regulate foreign investments in U.S. businesses and access by foreign persons to technology developed and produced in the United States. These laws include Section 721 of the Defense Production Act of 1950, as amended by the Foreign Investment Risk Review Modernization Act of 2018, and the regulations at 31 C.F.R. Parts 800 and 801, as amended, administered by the Committee on Foreign Investment in the United States; and the Export Control Reform Act of 2018, which is being implemented in part through Commerce Department rulemakings to impose new export control restrictions on "emerging and foundational technologies" yet to be fully identified. Application of these laws, including as they are implemented through regulations being developed, may negatively impact our business in various ways, including by restricting our access to capital and markets; limiting the collaborations we may pursue; regulating the export our products, services, and technology from the United States and abroad; increasing our costs and the time necessary to obtain required authorizations and to ensure compliance; and threatening monetary fines and other penalties if we do not.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, ("FCPA"), the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties to sell our products outside the United States, to conduct clinical trials, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new or existing product candidates from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and accept payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drug candidates to be reviewed and/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 to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Risks Related to Our Financial Condition and Need for Additional Capital

We have incurred significant losses since our inception and we expect to incur losses for the foreseeable future.

We have no products approved for commercial sale and have not generated any revenue to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred significant losses in each period since our inception in January 2017. For the nine months ended September 30, 2023 and 2022, we reported net losses of \$96.6 million and \$89.0 million, respectively. For the years ended December 31, 2022 and 2021, we reported net losses of \$112.0 million and \$100.8 million, respectively. As of September 30, 2023, we had an accumulated deficit of \$518.9 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, our product candidate. We anticipate that our expenses will increase substantially if, and as, we:

- conduct larger scale clinical trials for our product candidate, EFX, and any future product candidates;
- discover and develop new product candidates, and conduct nonclinical studies and clinical trials;
- incur any disruption or delays to the supply of our product candidate;
- manufacture, or have manufactured, clinical and commercial supplies of our product candidates;
- seek regulatory approvals for EFX or any future product candidates;
- commercialize EFX or any future product candidates, if approved;
- attempt to transition from a company with a development focus to a company capable of supporting commercial activities, including establishing sales, marketing and distribution infrastructure;
- hire additional clinical, scientific, and management personnel;
- add operational, financial, and management information systems and personnel;
- identify additional compounds or product candidates and acquire rights from third parties to those compounds or product candidates through licenses; and
- incur additional costs associated with operating as a public company.

Even if we succeed in commercializing EFX or any future product candidates, we may continue to incur substantial research and development and other expenditures to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We currently have a limited operating history, have not generated any revenue to date, and may never become profitable.

We are a clinical-stage biotechnology company with a limited operating history. Our operations to date have been limited to organizing and staffing our company, acquiring, developing and securing our technology and product candidate, EFX, and conducting nonclinical studies and clinical trials of EFX. We have not yet demonstrated our ability to complete late-stage clinical trials, obtain regulatory approval, formulate and manufacture a commercial-scale product, or conduct sales and marketing activities necessary for successful product commercialization. Investment in biotechnology product development is highly speculative because it entails substantial upfront expenditures in clinical research organizations and contract manufacturing organizations and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. Consequently, any predictions you may make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Though Phase 3 clinical development of EFX has been initiated, we do not expect to receive revenue from EFX for a number of years, if ever. To date, we have not generated any revenue and we will not be able to generate product revenue unless and until EFX, or any future product candidate, successfully completes clinical trials, receives regulatory approval, and is commercialized. We may seek to obtain revenue from collaboration or licensing agreements with third parties. Our ability to generate future product revenue from EFX or any future product candidates also depends on a number of additional factors, including our, or our current and future contractors' and collaborators', ability to:

- successfully complete nonclinical studies and clinical trials for EFX and any future product candidates;
- seek and obtain marketing approvals for any product candidates that complete clinical development;
- establish and maintain supply and manufacturing relationships with third parties, and ensure adequate and legally compliant manufacturing of bulk drug substances and drug products to maintain that supply;
- launch and commercialize any product candidates for which we obtain marketing approval, and, if launched independently, successfully establish a sales, marketing and distribution infrastructure;
- demonstrate the necessary safety data post-approval to ensure continued regulatory approval;
- obtain coverage and adequate product reimbursement from third-party payors, including government payors;
- achieve market acceptance for any approved products;
- address any competing technological and market developments;
- maintain our rights under our existing license agreement with Amgen and any similar agreements we may enter into in the future;
- negotiate favorable terms in any collaboration, licensing or other arrangements into which we may enter in the future and performing our obligations in such collaborations;
- establish, maintain, protect and enforce our intellectual property rights; and
- attract, hire and retain qualified personnel.

In addition, because of the numerous risks and uncertainties associated with biotechnology product development, including that our product candidate may not advance through development or achieve the endpoints of applicable clinical trials, we are unable to predict the timing or amount of increased expenses, or if or when we will achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we decide, or are required by the FDA or foreign regulatory authorities, to perform nonclinical studies or clinical trials in addition to those that we currently anticipate. Even if we complete the development and regulatory processes described above, we anticipate incurring significant costs associated with launching and commercializing any approved product.

If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

We will require additional capital to finance our operations, which may not be available to us on acceptable terms, or at all. As a result, we may not complete the development and commercialization of our product candidate or develop any future product candidates.

As a research and development company, our operations have consumed substantial amounts of cash since inception. We expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance EFX into later-stage clinical development.

As of September 30, 2023, we had \$613.0 million of cash, cash equivalents, short-term and long-term marketable securities. We raised gross proceeds of \$105.8 million from our initial public offering in June 2019 and \$216.4 million from a follow-on public offering in July 2020. We also raised gross proceeds of \$25.0 million from Pfizer through a registered direct common stock offering and borrowed \$10.0 million from Hercules under a term loan in June 2022. In September 2022, we raised gross proceeds of \$230.0 million from a follow-on public offering. In March 2023, we borrowed \$15.0 million from Hercules under our term loan facility. In April and May 2023, we raised gross proceeds of \$127.4 million from sales of common stock under an ATM offering and gross proceeds of \$220.0 million from sales of common stock through an underwritten registered direct offering. Any forecast of the period of time through which our financial resources will adequately support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this "Risk Factors" section. The assumptions underlying any estimate may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements, both short and long-term, will depend on many factors, including, but not limited to:

- the initiation, progress, timing, costs and results of nonclinical studies and clinical trials for our product candidate or any future product candidates we may develop;
- the cost and timing of manufacturing our product candidate for use in clinical trials or, if approved by the FDA, for commercial use;
- our ability to maintain our license to EFX from Amgen;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more nonclinical studies or clinical trials than those that we currently expect or change their requirements on studies that had previously been agreed to;
- the cost to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing any patents or other intellectual property rights;
- the effect of competing technological and market developments;
- market acceptance of any approved product candidates, including product pricing, as well as product coverage and the adequacy of reimbursement by third-party payors;
- the cost of acquiring, licensing or investing in additional businesses, products, product candidates and technologies;
- the cost and timing of selecting, auditing and potentially validating a manufacturing site for commercial scale manufacturing;
- the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval and that we determine to commercialize; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems.

We do not have any committed external source of funds or other support for our development efforts and we cannot be certain that additional funding will be available on acceptable terms, or at all. Until we can generate sufficient revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, and other marketing or distribution arrangements. If we raise additional funds through public or private equity offerings, the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Further, to the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, your ownership interest will be diluted. If we raise additional capital through debt financing, we could be subject to fixed payment obligations and may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. We also could be required to seek collaborators for one or more of our current or any future product candidates at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our products or product candidates or one or more of our other research and development initiatives. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Risks Related to Our Indebtedness

Our operating activities may be restricted as a result of covenants related to our term loan obligation, which we may be required to repay in an event of default, which could have a materially adverse effect on our business.

On June 15, 2022, we entered into a Loan and Security Agreement ("Loan Agreement") with Hercules Capital, Inc., ("Hercules") for an aggregate principal amount of up to \$100.0 million. Until we have repaid such indebtedness, the Loan Agreement subjects us to various customary covenants, including requirements as to financial reporting and insurance, and restrictions on our ability to dispose of our business or property, to change our line of business, to liquidate or dissolve, to merge or consolidate with any other entity or to acquire all or substantially all the capital stock or property of another entity, to incur additional indebtedness, to incur liens on our property, to pay any dividends or other distributions on capital stock other than dividends payable solely in capital stock, to redeem capital stock, to enter into licensing agreements, to engage in transactions with affiliates, or to encumber our intellectual property. Additionally, there is a financial covenant requiring us to maintain a minimum cash balance in relation to the outstanding principal balance of the Term Loan. Our business may be adversely affected by these restrictions on our ability to operate our business.

Additionally, we may be required to repay the outstanding indebtedness under the Term Loan if an event of default occurs under the Loan Agreement. Under the Loan Agreement, an event of default will occur if, among other things: we fail to make payments under the Loan Agreement; we breach any of our covenants under the Loan Agreement, subject to specified cure periods with respect to certain breaches; the Lender determines that a material adverse change has occurred; we or our assets become subject to certain legal proceedings, such as bankruptcy proceedings; we are unable to pay our debts as they become due; or we default on contracts with third parties which would permit the holder of indebtedness to accelerate the maturity of such indebtedness or that could have a material adverse change on us. As a result of the occurrence of an event of default, Hercules could accelerate all of the amounts due. In the event of an acceleration of amounts due under the Term Loan, we may not have enough available cash or be able to raise additional funds through equity or debt financings to repay such indebtedness at the time any such event of default occurs. In this case, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant to others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our business, financial condition and results of operations could be materially adversely affected as a result of any of these events.

Our level of indebtedness and debt service obligations could adversely affect our financial condition and may make it more difficult for us to fund our operations.

The Term Loan with Hercules provides up to \$100.0 million of debt financing and has interest-only payments through July 1, 2024, which may be extended based on achievement of certain milestones. Thereafter, we are obligated to make payments that will include installments of principal and interest through the maturity date of January 1, 2027.

This indebtedness may create additional financing risk for us, particularly if our business or prevailing financial market conditions are not conducive to paying off or refinancing our outstanding debt obligations at maturity. This indebtedness could also have important negative consequences, including the fact that:

- we will need to repay our indebtedness by making payments of interest and principal, which will reduce the amount of money available to finance our operations, our research and development efforts and other general corporate activities; and
- our failure to comply with the restrictive covenants in the Term Loan could result in an event of default that, if not cured or waived, would accelerate our obligation to repay this indebtedness, and Hercules could seek to enforce our security interest in the assets securing such indebtedness.

Risks Related to Commercialization and Market Acceptance

Risks Related to Commercialization

Even if we commercialize EFX or any future product candidates, if approved, these products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which could harm our business.

The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay or limit our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenue we generate from the sale of the product in that particular country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidate or any future product candidates obtain marketing approval.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors such as government health administration authorities, private health insurers and other organizations. Third-party payors determine which medications they will cover and establish reimbursement levels. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval, if any. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which marketing approval is obtained, if any.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates third-party payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidate or any future product candidates in human clinical trials and will face an even greater risk if we commercialize any resulting products. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, their family members, healthcare providers or others using, administering or selling our products. If we cannot successfully defend ourselves against claims that our product candidate or any future product candidates or products that we may develop caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- termination of clinical trial sites or entire trial programs;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial subjects or patients;
- loss of revenue;
- diversion of management and scientific resources from our business operations;
- the inability to commercialize any products that we may develop; and
- a decline in our stock price.

Our clinical trial liability insurance coverage may not adequately cover all liabilities that we may incur. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Our inability to obtain product liability insurance at an acceptable cost or to otherwise protect against potential product liability claims could prevent or delay the commercialization of any products or product candidates that we develop. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain marketing approval for our product candidate or any future product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. Large judgments have been awarded in lawsuits based on drugs that had unanticipated side effects. If we are sued for any injury caused by our products, product candidates or processes, our liability could exceed our product liability insurance coverage and our total assets. Claims against us, regardless of their merit or potential outcome, may also generate negative publicity or hurt our ability to obtain physician adoption of our product or expand our business.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.

We do not currently have an infrastructure for the sales, marketing, and distribution of pharmaceutical products. In order to market our product candidates, if approved by the FDA or any other regulatory body, we must build our sales, marketing, managerial, and other non-technical capabilities, or make arrangements with third parties to perform these services. There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively and they could expose our company to regulatory enforcement and legal risk in the execution of their sales and commercialization activities. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates if approved.

If we are unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition, and prospects will be materially adversely affected.

Our product candidate or any future product candidates may not achieve adequate market acceptance among physicians, patients, third-party payors and others in the medical community necessary for commercial success.

Even if our product candidate or any future product candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, third-party payors, pharmaceutical companies and others in the medical community. Demonstrating the safety and efficacy of our product candidate or any future product candidates and obtaining regulatory approvals will not guarantee future revenue. Our commercial success also depends on coverage and adequate reimbursement of our product candidate or any future product candidates by third-party payors, including government payors and private insurers, which may be difficult or time-consuming to obtain, may be limited in scope and may not be obtained in all jurisdictions in which we may seek to market our products. Third-party payors closely examine medical products to determine whether they should be covered by reimbursement and, if so, the level of reimbursement that will apply. We cannot be certain that third-party payors will sufficiently reimburse sales of our product or enable us to sell our product at a profitable price. Similar concerns could also limit the reimbursement amounts that health insurers or government agencies in other countries are prepared to pay for our products. In many regions, including Europe, Japan and Canada, where we may market our products, the pricing of prescription drugs is controlled by the government or regulatory agencies. Regulatory agencies in these countries could determine that the pricing for our products should be based on prices of other commercially available drugs for the same disease, rather than allowing us to market our products at a premium as new drugs. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

- the efficacy and safety profile of the product candidate as demonstrated in clinical trials;
- the timing of market introduction of the product candidate as well as competitive products;
- the clinical indications for which the product candidate is approved;
- acceptance of the product candidate as a safe and effective treatment by clinics and patients;

- the potential and perceived advantages of the product candidate over alternative treatments, including any similar generic treatments;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement and pricing by third-party payors;
- the relative convenience and ease of administration;
- the frequency and severity of adverse events;
- the effectiveness of sales and marketing efforts; and
- unfavorable publicity relating to our product candidate or any future product candidates.

Sales of medical products also depend on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective and cost effective as compared with competing treatments. If any product candidate is approved but does not achieve an adequate level of acceptance by such parties, we may not generate or derive sufficient revenue from that product candidate and may not become or remain profitable.

Risks Related to Our Operations

We incur significant costs and expend significant time and effort, as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

We incur significant legal, accounting and other expenses, and expend significant time and effort by management and other personnel, to comply with the rules applicable to us as a public company. We are subject to the reporting requirements of Nasdaq and of the Securities Exchange Act of 1934, as amended, which require, among other things, that we file with the Securities and Exchange Commission (SEC), annual, quarterly, and current reports with respect to our business and financial condition and that we establish and maintain effective disclosure controls, procedures and corporate governance practices. We must also comply with the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), and specifically Section 404 of the Sarbanes-Oxley Act, which requires that we establish and maintain effective internal controls over financial reporting. In order to maintain compliance with the SEC's rules that implement Section 404 of the Sarbanes-Oxley Act, we are required to make a formal assessment of the effectiveness of our internal control over financial reporting, to certify financial and other information in our quarterly and annual reports and to provide an annual management report on the effectiveness of our internal control over financial reporting, which includes the disclosure of any material weaknesses and associated remediation activities. When we are no longer a smaller reporting company, we will incur additional significant costs to meet the requirement to provide an attestation report on our internal control over financial reporting from our independent registered public accounting firm. We will need to continue to dedicate significant internal resources and outside consultants in order to complete management's annual assessment and to prepare for when we are no longer a smaller reporting company. Despite these efforts, there is no guarantee that we will be able to conclude that our internal controls over financial reporting remain effective.

Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (the Dodd-Frank Act) was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas, such as "say on pay" and proxy access. Stockholder activism, the current political environment, and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies, and the additional compliance requirements that we will be subject to when we are no longer a smaller reporting company, to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition, and results of operations. The increased costs will decrease our net income or increase our net loss and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain key financial or management personnel.

If we fail to maintain an effective system of internal controls over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, or any subsequent 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 financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could harm our business and have a negative effect on the trading price of our stock.

If material weaknesses or significant deficiencies in our internal control over financial reporting are identified in the future, we may not detect or remediate errors on a timely basis and our consolidated financial statements may be materially misstated. We, or our independent registered public accounting firm, may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from NASDAQ or other adverse consequences that would materially harm our business.

Our business and operations would suffer in the event of computer system failures, cyber-attacks or deficiencies in our or related parties' cyber security.

Given our limited operating history, we are still in the process of implementing our internal security measures. Our internal computer systems and those of current and future third parties on which we rely may fail and are vulnerable to damage from computer viruses and unauthorized access. Geopolitical instability, including Russia's invasion of Ukraine may increase cyber-attacks. Additionally, cyberattacks could include industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, including ransomware, denial-of-service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial, or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. Our information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines and connection to the Internet, face the risk of systemic failure that could disrupt our operations. A successful cyberattack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. While we have not, to our knowledge, experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in the following, which could be material:

- delays in our regulatory approval efforts;
- remediation costs, such as liability for stolen assets or information, repairs of system damage, and incentives to business partners in an effort to maintain relationships after an attack;
- investigation costs, including costs associated with potential notification of the attack to data subjects, regulators or others and costs to engage third party forensic investigators and other experts;
- increased cybersecurity protection costs, which may include the costs of making organizational changes, deploying additional personnel and protection technologies, training employees, and engaging third party experts and consultants;
- increased insurance premiums;
- reputational damage that adversely affects customer or investor confidence;
- damage to the company's competitiveness, stock price, and long-term shareholder value; and
- significantly increase our costs to recover or reproduce the data.

Likewise, we currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidate or any future product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. We rely on these third parties to implement effective security measures and identify and correct for any failures, deficiencies or breaches. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidate or any future product candidates could be hindered or delayed.

We use and generate materials that may expose us to material liability.

Our research programs involve the use of hazardous materials and chemicals, which are currently only handled by third parties. We are subject to foreign, federal, state and local environmental and health and safety laws and regulations governing, among other matters, the use, manufacture, handling, storage and disposal of hazardous materials and waste products. We may incur significant costs to comply with these current or future environmental and health and safety laws and regulations. In addition, we cannot completely eliminate the risk of contamination or injury from hazardous materials and may incur material liability as a result of such contamination or injury. In the event of an accident, an injured party may seek to hold us liable for any damages that result. Any liability could exceed the limits or fall outside the coverage of our workers' compensation, property and business interruption insurance and we may not be able to maintain insurance on acceptable terms, if at all. We currently carry no insurance specifically covering environmental claims.

General Risk Factors***Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.***

Our results of operations could be adversely affected by economic and political changes in the location in which we, or our suppliers and vendors, maintain operations. For example, our business may be generally exposed to the impact of political or civil unrest or military action. While we do not have direct exposure to Ukraine or Russia, we do have third-party manufacturing partners with locations in Europe, which may be affected by the ongoing conflict between Russia and Ukraine. In addition, we currently plan to activate sites for our SYNCHRONY trials in Israel and Turkey in 2024. These plans may be materially impacted or delayed by the ongoing armed conflict in Israel and the Gaza Strip and could result in difficulties securing necessary clearance from regulatory authorities, activating clinical trial sites, and screening and enrolling patients in such areas on schedule. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Our business is affected by macroeconomic conditions, including rising inflation, interest rates and supply chain constraints.

Various macroeconomic factors could adversely affect our business and the results of our operations and financial condition, including changes in inflation, interest rates and overall economic conditions and uncertainties such as those resulting from the current and future conditions in the global financial markets. For instance, rising interest rates have impacted the Company's net income. Recent supply chain constraints have led to higher inflation, which if sustained could have a negative impact on the Company's product development and operations. If inflation or other factors were to significantly increase our business costs, our ability to develop our current pipeline and new therapeutic products may be negatively affected. Interest rates, the liquidity of the credit markets and the volatility of the capital markets could also affect the operation of our business and our ability to raise capital on favorable terms, or at all, in order to fund our operations. Similarly, these macroeconomic factors could affect the ability of our third-party suppliers and manufacturers to manufacture clinical trial materials for our product candidates.

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults or non-performance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations and its financial condition and results of operations.

Adverse developments that affect financial institutions, such as events involving liquidity that are rumored or actual, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank (“SVB”) was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation (“FDIC”) as receiver. Although we are not a borrower or party to any such instruments with SVB, or any other financial institution currently in receivership, if Hercules, or any of our future lenders or counterparties to any such instruments were to be placed into receivership, we may be unable to access such funds.

Although we have not experienced any adverse impact to our liquidity or to our current and projected business operations, financial condition or results of operations, uncertainty remains over liquidity concerns in the broader financial services industry, and our business, our business partners, or industry as a whole may be adversely impacted in ways that we cannot predict at this time. Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. There is no guarantee that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion.

Although we assess our banking relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that us, the financial institutions with which we have credit agreements or arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry.

The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following:

- Delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;
- Potential or actual breach of contractual obligations that require us to maintain letters or credit or other credit support arrangements;
- Potential or actual breach of financial covenants in our credit agreements or credit arrangements; or
- Termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, widespread investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and/or projected business operations and financial condition and results of operations.

We are no longer a "smaller reporting company" as defined by the SEC, and the reduced disclosure requirements applicable to smaller reporting companies will not apply to us after December 31, 2023.

As of June 30, 2023, the market value of our common stock that was held by non-affiliates exceeded \$700 million, and as a result, as of December 31, 2023, we will no longer qualify as a "smaller reporting company" or as a "non-accelerated filer." As such, we will incur significant additional expenses in complying with the Sarbanes-Oxley Act of 2002 and rules implemented by the SEC. As a large accelerated filer, we will be subject to certain disclosure requirements that are applicable to other public companies that were not applicable to us as a smaller reporting company. These requirements include:

- compliance with the auditor attestation requirements of Section 404;
- compliance with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- full disclosure obligations regarding executive compensation; and
- compliance with the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

If we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources. Additionally, we expect that our loss of "smaller reporting company" status will require additional attention from management and will result in increased costs to us, which could include higher legal fees, accounting fees and fees associated with investor relations activities, among others.

Risks Related to an Investment in Our Securities

The market price of our stock may be volatile, and you could lose all or part of your investment. Because of potential volatility in our trading price and trading volume, we may incur significant costs from class action securities litigation.

The trading price of our common stock is likely to be volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. For example, between January 1, 2023 and October 31, 2023, our stock price has ranged from \$11.25 to \$58.38. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Quarterly Report on Form 10-Q, these factors include:

- developments associated with our license with Amgen, including any termination or other change in our relationship with Amgen;
- the success of competitive products or technologies;
- regulatory actions with respect to our product candidate or any future product candidates or our competitors' product candidates or products;
- results of clinical trials of our product candidate or any future product candidates or those of our competitors;
- actual or anticipated changes in our growth rate relative to our competitors;
- announcements by us or our competitors or collaborators of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- regulatory, legal or payor developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidate or any future product candidates or clinical development programs;
- the results of our efforts to in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;

- sales of our common stock by us, our insiders or our other stockholders;
- changes in the structure of healthcare payment systems;
- general economic, industry and market conditions;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad (such as the ongoing conflict between Ukraine and Russia, including the sanctions imposed by the United States, the EU and others on Russia and other related parties);
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic, industry and market conditions.

In addition, the stock market in general, and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, which has resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Although the markets recovered, market and industry factors, including potentially worsening economic conditions and other adverse effects or developments relating to inflation, rising interest rates, may significantly reduce the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this “Risk Factors” section, could have a dramatic and material adverse impact on the market price of our common stock.

Holders of stock in companies that have a volatile stock price frequently bring securities class action litigation against the company that issued the stock. We may be the target of this type of litigation in the future. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. A stockholder lawsuit could also divert the time and attention of our management. Securities litigation against us could result in substantial costs and divert our management’s attention from other business concerns, which could seriously harm our business.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company or if they cease to cover our company, the trading price for our stock would likely be negatively impacted. In the event that securities or industry analysts initiate coverage, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. In addition, if our operating results fail to meet the forecast of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Risks Related to Our Charter and Bylaws

Anti-takeover provisions under our organizational documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our fourth amended and restated certificate of incorporation and second amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of the stockholders may be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office, and special meetings of stockholders may not be called by any other person or persons;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds (2/3) of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than a majority of all outstanding shares of our voting stock to amend any bylaws by stockholder action and not less than two-thirds (2/3) of all outstanding shares of our voting stock to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval, which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our fourth amended and restated certificate of incorporation and second amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

Our amended and restated bylaws designate 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 amended and restated bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our second amended and restated bylaws (including the interpretation, validity or enforceability thereof), or (iv) any action asserting a claim that is governed by the internal affairs doctrine (the “Delaware Forum Provision”). The Delaware Forum Provision will not apply to any causes of action arising under the Exchange Act. Our amended and restated bylaws further provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the “Federal Forum Provision”). In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the U.S. federal securities laws and the rules and regulations thereunder.

The Delaware Forum Provision and the Federal Forum Provision in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, these forum selection clauses may limit our stockholders’ ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are “facially valid” under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the United States may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

Changes in tax laws could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be promulgated or issued under existing or new tax laws, which could result in an increase in our or our stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2022, we had U.S. federal and state net operating loss ("NOL") carryforwards of \$248.4 million and \$235.5 million, respectively and federal and state research and development tax credit carryforwards of \$8.9 million and \$1.2 million, respectively. If not utilized, such NOL carryforwards (other than federal NOL carryforwards arising in taxable years beginning after December 31, 2017) and research and development credits will expire at various dates beginning in 2037 and 2033, respectively. Our ability to use our U.S. federal and state NOL and tax credit carryforwards to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income. We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we may never achieve profitability. These NOL and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the current law, federal NOL carryforwards generated in tax years beginning after December 31, 2017 are not subject to expiration. However, any such NOL carryforwards may only offset 80% of our annual taxable income in taxable years beginning after December 31, 2020. In addition, under Sections 382 and 383 of the Code, the amount of benefits from our NOL carryforwards may be impaired or limited if we incur a cumulative ownership change of more than 50 percentage points by certain stockholders, as interpreted by the U.S. Internal Revenue Service, over a three-year period. We experienced such ownership changes on March 24, 2017, June 7, 2018 and July 8, 2020. We may experience ownership changes again in the future, some of which may be outside our control. No ownership change occurred in 2022. As a result, our use of federal NOL and tax credit carryforwards could be limited. State NOL carryforwards may be similarly limited. Any such disallowances may result in greater tax liabilities than we would incur in the absence of such a limitation and any increased liabilities could adversely affect our business, results of operations, financial position and cash flows.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

During the three and nine months ended September 30, 2023, we did not issue or sell any unregistered securities not previously disclosed in a Quarterly Report on Form 10-Q or in a Form 10-K.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

None.

EXHIBIT INDEX

<u>Exhibit Number</u>	<u>Exhibit Description</u>
3.1	Fourth Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K (File No. 001-38944) filed on June 24, 2019)
3.2	Amended and Restated Bylaws of the Registrant and the amendments thereto, as currently in effect (incorporated by reference to Exhibit 3.2 of the Registrant's Current Report on Form 8-K (File No. 001-38944) filed on March 12, 2021)
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended
32.1+	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	Inline XBRL Instance Document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101*)

* Filed herewith.

+ The certifications furnished in Exhibit 32.1 hereto are deemed to be furnished with this Quarterly Report on Form 10-Q and will not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

AKERO THERAPEUTICS, INC.

Date: November 13, 2023

By:

/s/ ANDREW CHENG

Andrew Cheng, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: November 13, 2023

By:

/s/ WILLIAM WHITE

William White
Executive Vice President, Chief Financial Officer and
Head of Corporate Development
(Principal Financial and Accounting Officer)

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO EXCHANGE ACT RULES 13a-14(a) AND 15d-14(a),
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Andrew Cheng, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Akero Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 13, 2023

/s/ ANDREW CHENG

Andrew Cheng, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO
RULES 13A-14(A) AND 15D-14(A) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, William White, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Akero Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 13, 2023

/s/ WILLIAM WHITE

William White

Executive Vice President, Chief Financial Officer and Head of Corporate
Development
(Principal Financial and Accounting Officer)

CERTIFICATION OF CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Andrew Cheng, certify pursuant to Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the “Exchange Act”) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that the Quarterly Report on Form 10-Q of Akero Therapeutics, Inc. for the quarterly period ended September 30, 2023, fully complies with the requirements of Section 13(a) or 15(d) of the Exchange Act and that the information contained in such Quarterly Report on Form 10-Q fairly presents, in all material respects, the financial condition and result of operations of Akero Therapeutics, Inc.

Dated: November 13, 2023

/s/ ANDREW CHENG

Andrew Cheng, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

I, William White, certify pursuant to Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the “Exchange Act”) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that the Quarterly Report on Form 10-Q of Akero Therapeutics, Inc. for the quarterly period ended September 30, 2023, fully complies with the requirements of Section 13(a) or 15(d) of the Exchange Act and that the information contained in such Quarterly Report on Form 10-Q fairly presents, in all material respects, the financial condition and result of operations of Akero Therapeutics, Inc.

Dated: November 13, 2023

/s/ WILLIAM WHITE

William White
Executive Vice President, Chief Financial Officer and Head of Corporate
Development
(Principal Financial and Accounting Officer)
