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

FORM 10-Q

(Mark One)

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

For the quarterly period ended 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 Number: 001-38978

FULCRUM THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**47-4839948**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
26 Landsdowne Street Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(Zip Code)**

(617) 651-8851
(Registrant's telephone number, including area code)

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 $0.001 per share	FULC	The Nasdaq Global 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	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☒

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

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

As of October 31, 2023, the registrant had 61,822,554 shares of common stock, $0.001 par value per share, outstanding.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements, which reflect our current views with respect to, among other things, our operations and financial performance. 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, objectives of management and expected market growth are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," “outlook,” "plan," "potential," "predict," "project," "should," "target," "would," and the negative version of these words and other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words and include, among other statements, express or implied statements regarding:

- our ongoing clinical trials of losmapimod and pociredir (formerly known as FTX-6058), including the effects of the revised inclusion and exclusion criteria on our trial of pociredir;
- the impact of our organizational streamlining and realignment of resources, including our anticipated cash runway;
- the initiation, timing, progress and results of our drug target discovery screening programs;
- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and our research and development programs;
- our plans to develop and, if approved, subsequently commercialize losmapimod, pociredir and any other product candidates, including in combination with other drugs and therapies;
- the timing of and our ability to submit applications for, and obtain and maintain regulatory approvals for losmapimod, pociredir and any other product candidates;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents, and marketable securities;
- the potential advantages of our product candidates;
- the rate and degree of market acceptance and clinical utility of our products, if our product candidates are approved;
- our estimates regarding the potential market opportunity for our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- the progress and results of our collaboration with MyoKardia, Inc., or MyoKardia, a wholly-owned subsidiary of Bristol-Myers Squibb Company, or under our recent exclusive global license agreement with CAMP4 Therapeutics Corp., or CAMP4;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- our estimates regarding expenses, future revenue, timing of any future revenue, capital requirements and needs for additional financing;
- the impact of government laws and regulations;
- the impact of a pandemic or an outbreak of highly infectious or contagious disease, such as the COVID-19 pandemic, on our business and operations, including our clinical trials and development plans, as well as our future financial results;
- our competitive position;
- developments relating to our competitors and our industry;
- our ability to maintain and establish collaborations or obtain additional funding; and
- our expectations regarding the time during which we will be an emerging growth company or a smaller reporting company as defined under the federal securities laws.

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. Such forward looking statements are subject to various risks and uncertainties. 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" and “Management’s Discussion and Analysis of Results of Operations” sections, that we believe 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 we may make or enter into.

You should read this Quarterly Report on Form 10-Q and the documents that we have filed as exhibits to this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Quarterly Report on Form 10-Q are made as of the date of this Quarterly Report on Form 10-Q, and 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 applicable law.

SUMMARY RISK FACTORS

Our business is subject to a number of risks that if realized could materially affect our business, financial condition, results of operations, cash flows and access to liquidity. These risks are discussed more fully in the “Risk Factors” section of this Quarterly Report on Form 10-Q. Our principal risks include the following:

- We have incurred significant losses since our inception. Our net loss was $109.9 million for the year ended December 31, 2022 and $72.6 million for the nine months ended September 30, 2023. We expect to incur losses over the next several years and may never achieve or maintain profitability. As of September 30, 2023, we had an accumulated deficit of $484.9 million.

- We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts. We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we continue our clinical trials of losmapimod and pociredir and continue research and development and initiate additional clinical trials of, and seek regulatory approval for, these and other product candidates.

- We are early in our development efforts, and we only have two product candidates in clinical trials. If we are unable to commercialize our product candidates or experience significant delays in doing so, such as the recent clinical hold on our clinical trial of pociredir, our business will be materially harmed.

- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. The results of preclinical studies and early clinical trials may not be predictive of future results. We may incur additional costs or experience further delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

- Because we are developing some of our product candidates for the treatment of diseases in which there is limited clinical experience and, in some cases, using new endpoints or methodologies, the U.S. Food and Drug Administration, or FDA, or other regulatory authorities may not consider the endpoints of our clinical trials to predict or provide clinically meaningful results.

- If serious adverse events or unacceptable side effects are identified during the development of our product candidates, including others’ product candidates in the same class of drugs, we may need to abandon or limit our development of some of our product candidates.

- We may not be successful in our efforts to use our proprietary technology to build a pipeline of product candidates.

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

- We rely, and expect to continue to rely, on contract manufacturing organizations, or CMOs, to manufacture our product candidates. If we are unable to enter into such arrangements as expected or if such organizations do not meet our supply requirements, development and/or commercialization of our product candidates may be delayed.

- We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, which may harm our business.

- We have entered into, and may in the future enter into, collaborations and license agreements with third parties for the discovery, development or commercialization of product candidates, including our collaboration with MyoKardia and our license agreement with CAMP4. If our collaboration is not successful or we are not able to develop product candidates that we license-in, we may not be able to capitalize on the market potential of these product candidates and our business could be adversely affected.

- If we are unable to obtain, maintain, enforce and protect patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.

- If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, or otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.

- 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 financial condition and results of operations.

- Our business was negatively impacted by the COVID-19 pandemic and may in the future be impacted by any future pandemics, as well as other geopolitical events that can impact our clinical trials or the supply chain, such as the Russian invasion of Ukraine or recent hostilities in Israel and Gaza Strip. These events may continue to, and any future pandemics may, adversely impact economies worldwide, which could result in adverse effects on our business and operations.

Table of Contents

In this Quarterly Report on Form 10-Q, unless otherwise stated or as the context otherwise requires, references to "Fulcrum," "Fulcrum Therapeutics," "the Company," "we," "us," "our" and similar references refer to Fulcrum Therapeutics, Inc. together with its consolidated subsidiary. The Fulcrum Therapeutics logo, FulcrumSeek and other trademarks or service marks of Fulcrum Therapeutics, Inc. appearing in this Quarterly Report on Form 10-Q are the property of Fulcrum Therapeutics, Inc. This Quarterly Report on Form 10-Q also contains registered marks, trademarks and trade names of other companies. All other trademarks, registered marks and trade names appearing herein are the property of their respective holders.

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

Fulcrum Therapeutics, Inc.

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	$ 30,080	$ 35,098
Marketable securities	227,011	167,823
Unbilled accounts receivable	580	229
Prepaid expenses and other current assets	4,819	4,369
Total current assets	262,490	207,519
Property and equipment, net	5,646	6,906
Operating lease right-of-use assets	7,661	9,063
Restricted cash	1,092	1,092
Other assets	1,990	2,105
Total assets	$ 278,879	$ 226,685
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,574	$ 3,638
Accrued expenses and other current liabilities	7,817	9,551
Deferred revenue, current portion	334	934
Operating lease liability, current	2,350	2,602
Total current liabilities	14,075	16,725
Operating lease liability, excluding current portion	9,145	10,821
Other liabilities, excluding current portion	197	197
Total liabilities	23,417	27,743
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized; no shares issued or outstanding	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized; 61,822,554 and 52,099,211 shares issued and outstanding as of September 30, 2023 and December 31, 2022, respectively	62	52
Additional paid-in capital	741,203	612,025
Accumulated other comprehensive loss	(886)	(797)
Accumulated deficit	(484,917)	(412,338)
Total stockholders' equity	255,462	198,942
Total liabilities and stockholders' equity	$ 278,879	$ 226,685

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

Fulcrum Therapeutics, Inc.

Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except per share data)

(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Collaboration revenue	$ 759	$ 1,183	$ 1,934	$ 5,657
Operating expenses:				
Research and development	18,238	15,366	52,802	58,216
General and administrative	9,961	9,707	31,804	31,564
Restructuring expenses	—	465	—	465
Total operating expenses	28,199	25,538	84,606	90,245
Loss from operations	(27,440)	(24,355)	(82,672)	(84,588)
Other income, net	3,423	617	10,093	852
Net loss	$ (24,017)	$ (23,738)	$ (72,579)	$ (83,736)
Net loss per share, basic and diluted	$ (0.39)	$ (0.51)	$ (1.19)	$ (1.97)
Weighted-average common shares outstanding, basic and diluted	61,823	46,213	61,121	42,603
Comprehensive loss:				
Net loss	$ (24,017)	$ (23,738)	$ (72,579)	$ (83,736)
Other comprehensive gain (loss):				
Unrealized gain (loss) on marketable securities	314	147	(89)	(524)
Total other comprehensive gain (loss)	314	147	(89)	(524)
Comprehensive loss	$ (23,703)	$ (23,591)	$ (72,668)	$ (84,260)

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

Fulcrum Therapeutics, Inc.

Consolidated Statements of Stockholders' Equity

(In thousands, except share amounts)

(Unaudited)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2021	40,626,224	41	514,362	(397)	(302,467)	211,539
Issuance of common stock under employee benefit plans	47,627	—	395	—	—	395
Vesting of restricted stock awards	9,754	—	—	—	—	—
Stock-based compensation expense	—	—	3,847	—	—	3,847
Unrealized loss on marketable securities	—	—	—	(693)	—	(693)
Net loss	—	—	—	—	(25,928)	(25,928)
Balance at March 31, 2022	40,683,605	$ 41	$ 518,604	$ (1,090)	$ (328,395)	$ 189,160
Issuance of common stock under employee benefit plans	324,180	—	2,764	—	—	2,764
Vesting of restricted stock awards	420	—	—	—	—	—
Stock-based compensation expense	—	—	2,879	—	—	2,879
Unrealized gain on marketable securities	—	—	—	22	—	22
Net loss	—	—	—	—	(34,070)	(34,070)
Balance at June 30, 2022	41,008,205	$ 41	$ 524,247	$ (1,068)	$ (362,465)	$ 160,755
Issuance of common stock in connection with public offering, net of issuance costs	11,029,410	11	80,793	—	—	80,804
Issuance of common stock under employee benefit plans	12,298	—	93	—	—	93
Stock-based compensation expense	—	—	3,353	—	—	3,353
Unrealized gain on marketable securities	—	—	—	147	—	147
Net loss	—	—	—	—	(23,738)	(23,738)
Balance at September 30, 2022	52,049,913	$ 52	$ 608,486	$ (921)	$ (386,203)	$ 221,414
Balance at December 31, 2022	52,099,211	$ 52	$ 612,025	$ (797)	$ (412,338)	198,942
Issuance of common stock in connection with public offering, net of issuance costs	9,615,384	10	117,336	—	—	117,346
Issuance of common stock under employee benefit plans	38,903	—	348	—	—	348
Vesting of restricted stock awards	5,496	—	—	—	—	—
Stock-based compensation expense	—	—	4,253	—	—	4,253
Unrealized gain on marketable securities	—	—	—	146	—	146
Net loss	—	—	—	—	(24,779)	(24,779)
Balance at March 31, 2023	61,758,994	$ 62	$ 733,962	$ (651)	$ (437,117)	$ 296,256
Issuance of common stock under employee benefit plans	50,912	—	141	—	—	141
Vesting of restricted stock awards	12,648	—	—	—	—	—
Stock-based compensation expense	—	—	3,363	—	—	3,363
Unrealized loss on marketable securities	—	—	—	(549)	—	(549)
Net loss	—	—	—	—	$ (23,783)	(23,783)
Balance at June 30, 2023	61,822,554	$ 62	$ 737,466	$ (1,200)	$ (460,900)	$ 275,428
Stock-based compensation expense	—	—	3,737	—	—	3,737
Unrealized gain on marketable securities	—	—	—	314	—	314
Net loss	—	—	—	—	$ (24,017)	(24,017)
Balance at September 30, 2023	61,822,554	$ 62	$ 741,203	$ (886)	$ (484,917)	$ 255,462

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

Fulcrum Therapeutics, Inc.

Consolidated Statements of Cash Flows

(In thousands)

(Unaudited)

	Nine Months Ended September 30,	
	2023	**2022**
Operating activities		
Net loss	$ (72,579)	$ (83,736)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	1,664	1,823
Stock-based compensation expense	11,353	10,079
Net (accretion of discounts) amortization of premiums on marketable securities	(4,663)	753
Changes in operating assets and liabilities:		
Accounts receivable	—	2,487
Unbilled accounts receivable	(351)	347
Prepaid expenses and other current assets	(450)	(936)
Operating lease assets and liabilities	(526)	(207)
Other assets	115	(1,556)
Accounts payable	(36)	(2,079)
Accrued expenses and other liabilities	(1,734)	(1,007)
Deferred revenue	(600)	(3,322)
Net cash used in operating activities	$ (67,807)	$ (77,354)
Investing activities		
Purchases of marketable securities	(169,818)	(67,864)
Maturities of marketable securities	115,203	118,486
Purchases of property and equipment	(431)	(1,847)
Net cash (used in) provided by investing activities	(55,046)	48,775
Financing activities		
Proceeds from issuance of common stock in connection with public offerings, net of issuance costs	117,345	80,853
Proceeds from issuance of common stock under benefit plans, net	490	3,252
Net cash provided by financing activities	117,835	84,105
Net (decrease) increase in cash, cash equivalents and restricted cash	(5,018)	55,526
Cash, cash equivalents, and restricted cash, beginning of period	36,190	36,504
Cash, cash equivalents, and restricted cash, end of period	$ 31,172	$ 92,030
Supplemental cash flow information		
Cash paid for operating lease liabilities	$ 2,489	$ 2,219
Non-cash investing and financing activities:		
Offering costs unpaid at end of period	$ —	$ 49
Property and equipment purchases unpaid at end of period	$ —	$ 20

The following table provides a reconciliation of the cash, cash equivalents, and restricted cash balances as of each of the periods shown above:

	September 30, 2023	**September 30, 2022**
Cash and cash equivalents	$ 30,080	$ 90,938
Restricted cash	1,092	1,092
Total cash, cash equivalents, and restricted cash	$ 31,172	$ 92,030

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

1. Nature of the Business and Basis of Presentation

Fulcrum Therapeutics, Inc. (the “Company” or “Fulcrum”) was incorporated in Delaware on August 18, 2015. The Company is focused on developing small molecules to improve the lives of patients with genetically-defined rare diseases in areas of high unmet medical need.

The Company is subject to a number of risks similar to other companies in the biotechnology industry, including, but not limited to, risks of failure of preclinical studies and clinical trials, dependence on key personnel, protection of proprietary technology, reliance on third party organizations, risks of obtaining regulatory approval for any product candidate that it may develop, development by competitors of technological innovations, compliance with government regulations, and the need to obtain additional financing. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing, and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance-reporting capabilities. Even if the Company’s development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States of America (“GAAP”). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Updates (“ASU”) of the Financial Accounting Standards Board (“FASB”).

The accompanying consolidated financial statements and footnotes to the financial statements have been prepared on the same basis as the most recently audited annual consolidated financial statements and, in the opinion of management, reflect all normal recurring adjustments necessary for the fair presentation of the Company’s financial position as of September 30, 2023 and the results of its operations and its cash flows for the three and nine months ended September 30, 2023 and 2022. 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. These consolidated financial statements should be read in conjunction with the Company’s audited consolidated financial statements and the notes thereto for the year ended December 31, 2022 included in the Company’s Annual Report on Form 10-K filed with the Securities and Exchange Commission (the “SEC”) on March 9, 2023 (the “Annual Report on Form 10-K”).

Sales of Common Stock

In January 2023, the Company completed a public offering of its common stock and issued and sold 9,615,384 shares of common stock at a public offering price of $13.00 per share, resulting in net proceeds of $117.3 million after deducting underwriting discounts and commissions and offering expenses.

Liquidity

The Company has incurred recurring losses and negative cash flows from operations since inception and has primarily funded its operations with proceeds from the sale of shares of its capital stock and from upfront payments received from the collaboration and license agreements with Acceleron Pharma Inc. (“Acceleron”), a wholly-owned subsidiary of Merck & Co., Inc. (“Merck”), and MyoKardia, Inc. (“MyoKardia”), a wholly owned subsidiary of Bristol Myers Squibb Company. As of September 30, 2023, the Company had an accumulated deficit of $484.9 million. The Company expects its operating losses and negative operating cash flows to continue into the foreseeable future as it continues to expand its research and development efforts. The Company expects to finance its future cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements.

The Company expects that its cash, cash equivalents, and marketable securities will be sufficient to fund its operating expenses and capital expenditure requirements for at least 12 months from the date of issuance of these financial statements. However, the Company has based this estimate on assumptions that may prove to be wrong, and its operating plan may change as a result of many factors currently unknown to it. As a result, the Company could deplete its capital resources sooner than it currently expects. If the Company is unable to raise additional funds through equity or debt financings when needed, it may be required to delay, limit, reduce or terminate development or future commercialization efforts or grant rights to develop and market product candidates that it would otherwise prefer to develop and market itself.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Fulcrum Therapeutics Securities Corp., which is a Massachusetts subsidiary created to buy, sell, and hold securities. All intercompany transactions and balances have been eliminated.

Summary of Significant Accounting Policies

The significant accounting policies and estimates used in the preparation of the accompanying consolidated financial statements are described in the Company’s audited consolidated financial statements for the year ended December 31, 2022 included in the Company’s Annual Report on Form 10-K. There have been no material changes in the Company’s significant accounting policies during the nine months ended September 30, 2023.

Use of Estimates

The preparation of financial statements in accordance with GAAP requires management to make certain estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the financial statements, and the reported amount of expenses during the reported periods. Estimates inherent in the preparation of these consolidated financial statements include, but are not limited to, estimates related to revenue recognition, accrued expenses, stock-based compensation expense, and income taxes. The Company bases its estimates on historical experience and other market specific or other relevant assumptions it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates as there are changes in circumstances, facts and experience. Actual results could differ from those estimates or assumptions.

Off-Balance Sheet Risk and Concentrations of Credit Risk

The Company has no significant off-balance sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents, marketable securities, and restricted cash. The Company’s cash, cash equivalents, and restricted cash are deposited in accounts at large financial institutions. The Company believes it is not exposed to significant credit risk due to the financial strength of the depository institutions in which the cash, cash equivalents and restricted cash are held. The Company maintains its cash equivalents in money market funds that invest in U.S. Treasury securities, U.S. Treasury securities, and commercial paper. The Company’s marketable securities consist of U.S. Treasury securities, corporate bonds, and commercial paper, and potentially subject the Company to concentrations of credit risk. The Company has adopted an investment policy that limits the amounts the Company may invest in any one type of investment. The Company has not experienced any credit losses and does not believe it is exposed to any significant credit risk on these funds.

Recent Accounting Pronouncements—Adopted

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. The standard requires that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, this standard requires allowances to be recorded instead of reducing the amortized cost of the investment. The Company adopted this guidance effective January 1, 2023. The adoption of this standard did not have a material impact on the Company's consolidated financial position and results of operations.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes-Simplifying the Accounting for Income Taxes*. The standard eliminates certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period, and the recognition of deferred tax liabilities for outside basis differences. The new guidance also simplifies aspects of the accounting for franchise taxes and enacted changes in tax laws or rates and clarifies the accounting for transactions that result in a step-up in the tax basis of goodwill. The Company adopted this guidance effective January 1, 2023. The adoption of this standard did not have a material impact on the Company's consolidated financial position and results of operations.

3. Fair Value Measurements

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicate the fair value hierarchy classification of such fair values as of September 30, 2023 and December 31, 2022 (in thousands):

	Fair Value Measurements at September 30, 2023			
	Total	**Level 1**	**Level 2**	**Level 3**
Cash equivalents:				
Money market funds	$ 17,336	17,336	—	—
U.S. Treasury securities	1,991	—	1,991	—
Commercial paper	10,753	—	10,753	—
Marketable securities:				
U.S. Treasury securities	19,516	—	19,516	—
Government agency securities	69,690	—	69,690	—
Commercial paper	32,552	—	32,552	—
Corporate bonds	105,253	—	105,253	—
Total	$ 257,091	$ 17,336	$ 239,755	$ —

	Fair Value Measurements at December 31, 2022			
	Total	**Level 1**	**Level 2**	**Level 3**
Cash equivalents:				
Money market funds	$ 25,174	$ 25,174	$ —	$ —
Commercial paper	9,924	—	9,924	—
Marketable securities:				
U.S. Treasury securities	10,231	—	10,231	—
Government agency securities	12,444	—	12,444	—
Commercial paper	48,476	—	48,476	—
Corporate bonds	96,672	—	96,672	—
Total	$ 202,921	$ 25,174	$ 177,747	$ —

There were no transfers between fair value levels during the three and nine months ended September 30, 2023.

4. Cash Equivalents and Marketable Securities

Cash equivalents and marketable securities consisted of the following as of September 30, 2023 and December 31, 2022 (in thousands):

	Fair Value Measurements at September 30, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 17,336	$ —	$ —	$ 17,336
U.S. Treasury securities	1,991	—	—	1,991
Commercial paper	10,757	—	(4)	10,753
Total cash equivalents	30,084	—	(4)	30,080
Marketable securities:				
U.S. Treasury securities	19,585	—	(69)	19,516
Government agency securities	69,986	—	(296)	69,690
Commercial paper	32,600	—	(48)	32,552
Corporate bonds	105,722	—	(469)	105,253
Total marketable securities	227,893	—	(882)	227,011
Total cash equivalents and marketable securities	$ 257,977	$ —	$ (886)	$ 257,091

	Fair Value Measurements at December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 25,174	$ —	$ —	$ 25,174
Commercial paper	9,928	—	(4)	9,924
Total cash equivalents	35,102	—	(4)	35,098
Marketable securities:				
U.S. Treasury securities	10,267	—	(36)	10,231
Government agency securities	12,493	—	(49)	12,444
Commercial paper	48,661	—	(185)	48,476
Corporate bonds	97,195	3	(526)	96,672
Total marketable securities	168,616	3	(796)	167,823
Total cash equivalents and marketable securities	$ 203,718	$ 3	$ (800)	$ 202,921

There were no sales of marketable securities during the three and nine months ended September 30, 2023. As of September 30, 2023, the Company held 83 debt securities that were in an unrealized loss position for less than 12 months with an aggregate fair value of $216.6 million. As of September 30, 2023, the Company held 5 debt securities that were in an unrealized loss position for greater than 12 months with an aggregate fair value of $10.4 million. As of September 30, 2023, the aggregate fair value of marketable securities with a remaining contractual maturity of greater than one year was $13.7 million.

The Company has the intent and ability to hold its debt securities until recovery. As a result, the Company did not record any charges for credit-related impairments for its marketable securities for the three and nine months ended September 30, 2023.

5. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	September 30, 2023	December 31, 2022
Lab equipment	$ 9,493	$ 9,057
Furniture and fixtures	786	786
Computer equipment	393	393
Software	199	199
Leasehold improvements	7,102	7,102
Construction in process	—	31
Total property and equipment	17,973	17,568
Less: accumulated depreciation	(12,327)	(10,662)
Property and equipment, net	$ 5,646	$ 6,906

Depreciation expense for the three months ended September 30, 2023 and 2022 was $0.5 million and $0.6 million, respectively. Depreciation expense for the nine months ended September 30, 2023 and 2022 was $1.7 million and $1.8 million, respectively.

6. Additional Balance Sheet Detail

Prepaid expenses and other current assets consisted of the following (in thousands):

	September 30, 2023	December 31, 2022
Prepaid expenses	$ 3,466	$ 3,425
Prepaid sign-on bonuses subject to vesting provisions	254	92
Interest income receivable	1,099	852
Total prepaid expenses and other current assets	$ 4,819	$ 4,369

Accrued expenses and other current liabilities consisted of the following (in thousands):

	September 30, 2023	December 31, 2022
External research and development	$ 3,107	$ 4,700
Payroll and benefits	4,023	4,211
Professional services	422	535
Other	265	105
Total accrued expenses and other current liabilities	$ 7,817	$ 9,551

7. Preferred Stock

As of September 30, 2023 and December 31, 2022, 5,000,000 shares of undesignated preferred stock were authorized. No shares of preferred stock were issued or outstanding as of September 30, 2023 and December 31, 2022.

No dividends have been declared since inception.

8. Common Stock

As of September 30, 2023 and December 31, 2022, 200,000,000 shares of common stock, $0.001 par value per share, were authorized.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are not entitled to receive dividends, unless declared by the Company's board of directors, subject to the preferential dividend rights of any preferred stock then outstanding. No dividends have been declared or paid by the Company since its inception.

As of September 30, 2023 and December 31, 2022, the Company has reserved for future issuance the following number of shares of common stock:

	September 30, 2023	December 31, 2022
Shares reserved for exercises of outstanding stock options	10,108,766	6,504,080
Shares reserved for vesting of restricted stock units	78,142	76,718
Shares reserved for future issuance under the 2019 Stock Incentive Plan	2,896,782	1,941,054
Shares reserved for future issuance under the 2019 Employee Stock Purchase Plan	1,438,938	1,061,279
Shares reserved for future issuance under the 2022 Inducement Stock Incentive Plan	1,003,472	329,880
	15,526,100	9,913,011

9. Stock-based Compensation Expense

2016 Stock Incentive Plan

In July 2016, the Company adopted the 2016 Stock Incentive Plan (the “2016 Plan”), which provided for the grant of restricted stock awards, restricted stock units, incentive stock options, non-statutory stock options, and other stock-based awards to the Company’s eligible employees, officers, directors, consultants, and advisors. As of the effective date of the 2019 Stock Incentive Plan (the “2019 Plan”), and as of September 30, 2023, no shares remained available for future issuance under the 2016 Plan. Any options or other awards outstanding under the 2016 Plan remain outstanding and effective.

2019 Stock Incentive Plan

On July 2, 2019, the Company’s stockholders approved the 2019 Plan, which became effective on July 17, 2019. The 2019 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards to the Company’s officers, employees, directors, consultants and advisors. The number of shares initially reserved for issuance under the 2019 Plan was 2,017,142 shares, plus the shares of common stock remaining available for issuance under the 2016 Plan as of July 17, 2019. The number of shares reserved was annually increased on January 1, 2020 and will be increased each January 1 thereafter through January 1, 2029 by the least of (i) 2,000,000 shares, (ii) 4% of the number of shares of the Company’s common stock outstanding on the first day of each such year or (iii) an amount determined by the Company’s board of directors. On January 1, 2023, the number of shares reserved for issuance under the 2019 Plan was increased by 2,000,000 shares. As of September 30, 2023, there were 2,896,782 shares available for future issuance under the 2019 Plan.

The shares of common stock underlying any awards that expire, terminate, or are otherwise surrendered, cancelled, forfeited or repurchased by the Company under the 2016 Plan or the 2019 Plan will be added back to the shares of common stock available for issuance under the 2019 Plan. As of July 17, 2019, no further awards will be made under the 2016 Plan.

2022 Inducement Stock Incentive Plan

In February 2022, the Company’s board of directors adopted the 2022 Inducement Stock Incentive Plan (the “Inducement Plan”), pursuant to which the Company may grant, subject to the terms of the Inducement Plan and Nasdaq rules, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units, and other stock-based awards. The Company initially reserved a total of 1,750,000 shares of common stock for the issuance of awards under the Inducement Plan. The number of shares reserved and available for issuance under the Inducement Plan can be increased at any time with the approval of the Company’s board of directors. The Inducement Plan permits the board of directors, a delegated committee of the board of directors, or a delegated officer of the Company to grant the stock-based awards available under the Inducement Plan to attract key employees for the growth of the Company. Effective March 8, 2023, the Company’s board of directors amended the Inducement Plan to increase the number of shares reserved for issuance by 2,000,000 shares. Effective May 18, 2023, the Company’s board of directors amended the Inducement Plan to increase the number of shares reserved for issuance by 1,400,000 shares. As of September 30, 2023, there were 1,003,472 shares available for future grant under the Inducement Plan.

Stock Options

Stock options granted by the Company typically vest over a four-year period and have a ten year contractual term. Shares issued upon the exercise of stock options are issued from the Company's pool of authorized but unissued common stock. In addition to stock options granted under the 2019 Plan and 2016 Plan, the Company has granted stock options as material inducements to employment in accordance with Nasdaq Listing Rule 5635(c)(4), which were granted outside of the 2019 Plan and 2016 Plan. The following table summarizes the Company's stock option activity during the nine months ended September 30, 2023:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2022	6,504,080	$ 11.99	8.55	$ 1,885,160
Granted	5,790,673	5.92		
Exercised	(38,903)	8.96		
Cancelled	(2,147,084)	11.96		
Outstanding at September 30, 2023	10,108,766	$ 8.53	8.71	$ 4,871,462
Exercisable at September 30, 2023	2,890,946	$ 12.74	7.29	$ —

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 as of the balance sheet date for those options that had exercise prices lower than the fair value of the Company's common stock.

The weighted average grant date fair value of stock options granted in the three and nine months ended September 30, 2023 was $3.26 per share and $4.67 per share, respectively. The weighted average grant date fair value of stock options granted in the three and nine months ended September 30, 2022 was $4.94 per share and $8.52 per share, respectively. The total intrinsic value of stock options exercised during the three and nine months ended September 30, 2023 was zero and $0.2 million, respectively. The total intrinsic value of stock options exercised during the three and nine months ended September 30, 2022 was less than $0.1 million and $2.6 million, respectively.

The fair value of stock options granted during the three and nine months ended September 30, 2023 and 2022 has been calculated on the date of grant using the following weighted average assumptions:

	Three Months Ended September 30, 2023	Three Months Ended September 30, 2022	Nine Months Ended September 30, 2023	Nine Months Ended September 30, 2022
Risk-free interest rate	4.1%	2.9%	3.7%	2.2%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%
Expected term (years)	6.1	6.1	6.1	6.0
Expected stock price volatility	100.4%	90.0%	98.4%	88.7%

Restricted Stock Units

The Company has also granted restricted stock units. The shares of common stock underlying restricted stock units typically vest over a four-year period. The shares of common stock are recorded in stockholders' equity as they vest.

The following table summarizes the Company's restricted stock unit activity during the nine months ended September 30, 2023:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2022	76,718	$ 9.73
Granted	37,045	12.59
Vested	(18,144)	9.79
Cancelled	(17,477)	10.75
Unvested at September 30, 2023	78,142	$ 10.84

Stock-based Compensation Expense

The total compensation cost recognized in the statements of operations and comprehensive loss associated with all stock-based compensation awards granted by the Company is as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
General and administrative	$ 2,734	$ 2,597	$ 8,533	$ 7,138
Research and development	1,003	756	2,820	2,941
Total stock-based compensation expense	$ 3,737	$ 3,353	$ 11,353	$ 10,079

As of September 30, 2023, the Company had an aggregate of $35.2 million of unrecognized stock-based compensation expense, which is expected to be recognized over a weighted average period of 3.07 years.

2019 Employee Stock Purchase Plan

On July 2, 2019, the Company's stockholders approved the 2019 Employee Stock Purchase Plan (the "ESPP"), which became effective on July 17, 2019. A total of 252,142 shares of common stock were initially reserved for issuance under the ESPP. In addition, the number of shares of common stock reserved under the ESPP was increased on January 1, 2020, and will be increased annually on each January 1 thereafter through January 1, 2029, by the least of (i) 428,571 shares of common stock, (ii) 1% of the number of shares of the Company's common stock outstanding on the first day of each such year or (iii) an amount determined by the Company's board of directors. On January 1, 2023, the number of shares reserved for issuance under the 2019 ESPP was increased by 428,571 shares. As of September 30, 2023, there were 1,438,938 shares available for future issuance under the ESPP.

10. Collaboration Agreements

Acceleron Collaboration Agreement

On December 20, 2019, the Company entered into the Acceleron Collaboration Agreement to identify biological targets to modulate specific pathways associated with a targeted indication within the pulmonary disease space (the "Indication"). Under the terms of the Acceleron Collaboration Agreement, the Company granted Acceleron an exclusive worldwide license under certain intellectual property rights to make, have made, use, sell, have sold, import, export, distribute and have distributed, market, have marketed, promote, have promoted, or otherwise exploit molecules and products directed against or expressing certain biological targets identified by the Company for the treatment, prophylaxis, or diagnosis of the Indication.

On June 3, 2022, Acceleron notified the Company of its termination of the Acceleron Collaboration Agreement for convenience, which became effective 120 days after the Company's receipt of the notice, or October 1, 2022.

During the three and nine months ended September 30, 2023, the Company recognized no collaboration revenue associated with the Acceleron Collaboration Agreement. During the nine months ended September 30, 2022, the Company recognized $1.0 million of collaboration revenue under the Acceleron Collaboration Agreement, which includes $0.6 million of revenue recognized that was included in deferred revenue as of December 31, 2021. During the three months ended September 30, 2022, the Company recognized no collaboration revenue under the Acceleron Collaboration Agreement. As of September 30, 2023 and December 31, 2022, the Company recorded no deferred revenue, unbilled accounts receivable, or accounts receivable associated with the Acceleron Collaboration Agreement. As of September 30, 2023 and December 31, 2022, the Company had received $4.9 million of cost reimbursement payment under the Acceleron Collaboration Agreement and $2.0 million associated with the achievement of specified research milestones.

MyoKardia Collaboration Agreement

On July 20, 2020, the Company entered into the MyoKardia Collaboration Agreement, as amended, pursuant to which the Company granted to MyoKardia an exclusive worldwide license under certain intellectual property rights to research, develop, make, have made, use, have used, sell, have sold, offer for sale, have offered for sale, import, have imported, export, have exported, distribute, have distributed, market, have marketed, promote, have promoted, or otherwise exploit products directed against certain biological targets identified by the Company that are capable of modulating up to a certain number of genes of interest with relevance to certain genetically defined cardiomyopathies.

Pursuant to a mutually agreed research plan, the Company will perform assay screening and related research activities to identify and validate up to a specified number of potential cardiomyopathy gene targets (“Identified Targets”) for further research, development, manufacture and commercialization by MyoKardia. The Company and MyoKardia will work together to determine how best to advance at each stage of the research activities under the research plan and to identify which of the Identified Targets, if any, meet the criteria set forth in the research plan (the “Cardiomyopathy Target Candidates”). Upon completion of the research plan, the parties will work together to prepare a final data package and MyoKardia may designate certain Cardiomyopathy Target Candidates for MyoKardia’s further exploitation under the MyoKardia Collaboration Agreement (the “Cardiomyopathy Targets”). If MyoKardia does not designate any Cardiomyopathy Targets during the designated period, then the MyoKardia Collaboration Agreement will automatically terminate. If MyoKardia designates one or more Cardiomyopathy Targets, then MyoKardia will be obligated to use commercially reasonable efforts to seek regulatory approval for and to commercialize one product directed against an Identified Target in certain specified countries.

During the period in which the Company is performing the research activities pursuant to the research plan (the “Research Term”) and for a specified period beyond the Research Term if MyoKardia designates a Cardiomyopathy Target, the Company may only use the data generated from such research activities for MyoKardia in accordance with the MyoKardia Collaboration Agreement. During the Research Term and for a specified period thereafter, the Company may not research, develop, manufacture, commercialize, use, or otherwise exploit any compound or product (a) that is a Compound or Product under the MyoKardia Collaboration Agreement that is directed against the Cardiomyopathy Target Candidates for the treatment, prophylaxis, or diagnosis of any indication or (b) for the treatment of any genetically defined cardiomyopathies shown to be related to certain specified genes of interest that are modulated by the Cardiomyopathy Targets.

Under the MyoKardia Collaboration Agreement, MyoKardia made a $10.0 million upfront payment and a $2.5 million payment as prepaid research funding to the Company in July 2020. MyoKardia will also reimburse the Company for the costs of the research activities not covered by the prepaid research funding, up to a maximum amount of total research funding (including the prepaid research funding). Upon the achievement of specified preclinical, development and sales milestones, the Company will be entitled to preclinical milestone payments, development milestone payments and sales milestone payments of up to $298.5 million in the aggregate per target for certain Identified Targets, and of up to $150.0 million in the aggregate per target for certain other Identified Targets. To date, the Company has achieved a $2.5 million specified preclinical milestone. MyoKardia will also pay the Company tiered royalties ranging from a mid single-digit percentage to a low double-digit percentage based on MyoKardia’s, and any of its affiliates’ and sublicensees’, annual worldwide net sales of products under the MyoKardia Collaboration Agreement directed against any Identified Target. The royalties are payable on a product-by-product basis during a specified royalty term, and may be reduced in specified circumstances.

The MyoKardia Collaboration Agreement continues on a country-by-country and product-by-product basis until the last to expire royalty term for a product, at which time the MyoKardia Collaboration Agreement expires with respect to such product in such country. Either party has the right to terminate the MyoKardia Collaboration Agreement if the other party has materially breached in the performance of its obligations under the MyoKardia Collaboration Agreement and such breach has not been cured within the applicable cure period. MyoKardia also has the right to terminate the MyoKardia Collaboration Agreement for convenience in its entirety or on a target-by-target, product-by-product or molecule-by-molecule basis.

Accounting Analysis

Identification of the Contract

The Company assessed the MyoKardia Collaboration Agreement and concluded that it represents a contract with a customer within the scope of ASC 606.

Identification of the Promises and Performance Obligations

The Company determined that the MyoKardia Collaboration Agreement contains the following promises: (i) an exclusive worldwide license under certain intellectual property rights, including rights to a specified number of potential cardiomyopathy gene targets identified by the Company for further research, development, manufacture and commercialization for the treatment, prophylaxis, or diagnosis of certain genetically defined cardiomyopathies that was conveyed at the inception of the arrangement (the “MyoKardia License”), (ii) research services to identify and validate potential biological targets (the “MyoKardia Research Services”), and (iii) participation in the joint steering committee (the “MyoKardia JSC”).

The Company assessed the above promises and concluded that the MyoKardia License is not capable of being distinct from the MyoKardia Research Services given that the MyoKardia License has limited value without the performance of the MyoKardia Research Services and the MyoKardia Research Services can only be performed by the Company due to their specialized nature. Therefore, the Company has concluded that the MyoKardia License and the MyoKardia Research Services represent a single combined performance obligation.

The Company also assessed the participation on the MyoKardia JSC and concluded that the promise is quantitatively and qualitatively immaterial in the context of the MyoKardia Collaboration Agreement. Accordingly, the Company has disregarded its participation on the MyoKardia JSC as a performance obligation.

Determination of the Transaction Price

The Company received a non-refundable upfront payment of $10.0 million, which the Company included in the transaction price. In December 2021, the Company achieved a $2.5 million specified preclinical milestone associated with the MyoKardia Collaboration Agreement, which was previously constrained due to the significant uncertainty regarding whether such preclinical milestone would be achieved. The Company included this amount in the transaction price as of December 31, 2021. Based on the continued uncertainty associated with the achievement of any of the remaining preclinical and development milestone payments that the Company is eligible to receive, the Company has constrained the variable consideration associated with those milestone payments and excluded them from the transaction price. As part of its evaluation of constraining the preclinical and development milestones, the Company considered numerous factors, including the fact that the achievement of the preclinical and development milestones are contingent upon the results of the underlying preclinical and development activities and are thus outside of the control of the Company.

The Company also included in the transaction price the expected amount of costs to be reimbursed for the MyoKardia Research Services, which includes the $2.5 million prepaid research funding payment that the Company received in the third quarter of 2020.

The Company reassesses the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjusts its estimate of the transaction price. There was no change in the amount of variable consideration constrained during the three and nine months ended September 30, 2023.

Any consideration related to sales milestone payments (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license granted to MyoKardia and therefore are recognized at the later of when the related sales occur or the performance obligation is satisfied.

Allocation of the Transaction Price to Performance Obligations

As noted above, the Company has identified a single performance obligation associated with the MyoKardia Collaboration Agreement. Therefore, the Company will allocate the entire amount of the transaction price to the identified single performance obligation.

Recognition of Revenue

The Company recognizes revenue related to the MyoKardia Collaboration Agreement over time as the MyoKardia Research Services are rendered. The Company has concluded that an input method is a representative depiction of the transfer of services under the MyoKardia Collaboration Agreement. The method of measuring progress towards the delivery of the services incorporates actual cumulative internal and external costs incurred relative to total internal and external costs expected to be incurred to satisfy the performance obligation. The period over which total costs are estimated reflects the Company's estimate of the period over which it will perform the MyoKardia Research Services. Changes in estimates of total internal and external costs expected to be incurred are recognized in the period of change as a cumulative catch-up adjustment.

During the three and nine months ended September 30, 2023, the Company recognized $0.8 million and $1.9 million, respectively, of collaboration revenue associated with the MyoKardia Collaboration Agreement, which includes $0.2 million and $0.6 million, respectively, of revenue recognized that was included in deferred revenue as of December 31, 2022. During the three and nine months ended September 30, 2022, the Company recognized $1.2 million and $4.7 million, respectively, of collaboration revenue associated with the MyoKardia Collaboration Agreement, which includes $0.4 million and $2.7 million, respectively, of revenue recognized that was in deferred revenue as of December 31, 2021. As of September 30, 2023 and December 31, 2022, the Company recorded deferred revenue of $0.3 million and $0.9 million, respectively, associated with the MyoKardia Collaboration Agreement, which is classified as either current or net of current portion in the accompanying consolidated balance sheets based on the period over which the revenue is expected to be recognized. The aggregate deferred revenue balance represents the aggregate amount of the transaction price allocated to the performance obligations that are unsatisfied as of September 30, 2023 and December 31, 2022. As of September 30, 2023, the Company had received $6.6 million of cost reimbursement payments under the MyoKardia Collaboration Agreement and $2.5 million associated with the achievement of a preclinical milestone. As of December 31, 2022, the Company had received $5.6 million of cost reimbursement payments under the MyoKardia Collaboration Agreement and $2.5 million associated with the achievement of a preclinical milestone. As of September 30, 2023, the Company recorded unbilled accounts receivable of $0.6 million related to reimbursable research and development costs under the MyoKardia Collaboration Agreement for activities performed during the three months ended September 30, 2023. As of December 31, 2022, the Company recorded unbilled accounts receivable of $0.2 million related to reimbursable research and development costs under the MyoKardia Collaboration Agreement for activities performed during the three months ended December 31, 2021. As of September 30, 2023 and December 31, 2022, the Company recorded no accounts receivable under the MyoKardia Collaboration Agreement.

11. License Agreements

GSK Agreement

In February 2019, the Company entered into the right of reference and license agreement, as amended (the "GSK Agreement"), with subsidiaries of GlaxoSmithKline plc (collectively referred to as "GSK"), pursuant to which the Company has been granted an exclusive worldwide license to develop and commercialize losmapimod. Under the GSK Agreement, the Company also acquired reference rights to relevant regulatory and manufacturing documents and GSK's existing supply of losmapimod drug substance and product. The Company also has the right to sublicense its rights under the license agreement, subject to certain conditions. The Company is obligated to use commercially reasonable efforts to develop and commercialize losmapimod at its sole cost. The Company is also responsible for costs related to the filing and maintenance of the licensed patent rights.

Under the GSK Agreement, the Company issued 12,500,000 shares of Series B Preferred Stock to GSK. In addition, the Company may owe GSK up to $37.5 million in certain specified clinical and regulatory milestones, including a $5.0 million milestone that was achieved during the second quarter of 2022 and a $2.5 million milestone previously achieved and paid during 2019, and up to $60.0 million in certain specified sales milestones. The Company agreed to pay tiered royalties on annual net sales of losmapimod that range from mid single-digit percentages to a low double-digit, but less than teens, percentage. The royalties are payable on a product-by-product and country-by-country basis, and may be reduced in specified circumstances.

The GSK Agreement may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, the GSK Agreement will continue in effect until the expiration of the Company's royalty obligations, which expire on a country-by-country basis on the later of (i) ten years after the first commercial sale in the country or (ii) approval of a generic version of losmapimod by the applicable regulatory agency.

The Company recognizes clinical and regulatory milestone payments when the underlying contingency is resolved and the consideration is paid or becomes payable. The milestone payments are capitalized or expensed depending on the nature of the associated asset as of the date of recognition.

CAMP4 Agreement

In July 2023, the Company entered into a license agreement (the "CAMP4 Agreement") with CAMP4 Therapeutics Corporation ("CAMP4") pursuant to which the Company received a worldwide exclusive license (including the right to sublicense) from CAMP4 to rights under its Diamond Blackfan Anemia ("DBA") program, which includes certain small molecule compounds, composition of matter and method of use patent rights, and know-how for the Company to research, develop, manufacture, use, commercialize or otherwise exploit therapeutic products in any indication, including the grant of a sublicense under certain intellectual property rights that CAMP4 has licensed under an agreement with Children's Medical Center Corporation ("CMCC").

The Company made an undisclosed upfront non-refundable, non-creditable payment to CAMP4. If the Company succeeds in developing and commercializing licensed products, CAMP4 will be eligible to receive (i) up to $35.0 million in development and regulatory milestone payments, and (ii) up to $35.0 million in sales milestone payments. CAMP4 is also eligible to receive royalties on worldwide net sales of licensed products ranging from mid-single digit to low-double digit, subject to potential reduction following loss of patent coverage, the launch of certain generic products or royalty stacking for licenses of third party intellectual property. The royalties will expire on a product-by-product and country-by-country basis upon the latest to occur of (i) the expiration of all valid patent claims covering the compounds in such country, (ii) the expiration of all regulatory exclusivities in such country, and (iii) 10 years following the first commercial sale of in such country. The Company is responsible for the costs associated with the development and regulatory approvals of licensed products.

Unless earlier terminated in accordance with its terms, the license agreement continues on a country-by-country and licensed product-by-licensed product basis until the expiration of the royalty term in each country, at which time the license agreement expires with respect to such licensed product in such country and the Company will have a fully-paid up, royalty-free and perpetual license to the licensed patent rights and know-how with respect to such licensed product in such country. CAMP4 has the right to terminate the license agreement in the event of the Company's non-payment (subject to cure periods and tolling for bona fide disputes). CAMP4 may also terminate the license agreement if the Company challenges certain patents sublicensed to the Company by CAMP4. Either party may terminate the license agreement in its entirety for the other party's material breach if such other party fails to cure the breach. Either party may also terminate the agreement in its entirety upon certain insolvency events involving the other party. The Company has the right to terminate the license agreement with CAMP4 for any or no reason upon prior written notice to CAMP4.

The Company recognizes development and regulatory milestone payments when the underlying contingency is resolved and the consideration is paid or becomes payable. The milestone payments are capitalized or expensed depending on the nature of the associated asset as of the date of recognition.

12. Leases

Operating Leases

26 Landsdowne Street

In November 2017, the Company entered into a lease agreement for its current corporate headquarters comprising approximately 28,731 square feet of office and laboratory space at 26 Landsdowne Street in Cambridge, Massachusetts, commencing December 2017. The Company began to occupy and use the leased space for its intended purpose in June 2018. The lease ends on June 30, 2028. The Company has the option to extend the term of the lease for an additional five-year period, at the market rate, by giving the landlord written notice of its election to exercise the extension at least nine months prior to the original expiration of the lease term. The lease has a total commitment of $25.1 million over the ten year term, and includes escalating rent payments. The lease provides the Company with an allowance for normal leasehold improvements of $5.0 million. The lease agreement requires the Company to either pay a security deposit or maintain a letter of credit of $1.1 million. The Company maintains a letter of credit for this lease and has recorded the cash held to secure the letter of credit as restricted cash on the consolidated balance sheet as of September 30, 2023 and December 31, 2022. Operating lease expense and variable lease expense associated with this lease for the three months ended September 30, 2023 was approximately $0.5 million and $0.2 million, respectively. Operating lease expense and variable lease expense associated with this lease for the nine months ended September 30, 2023 was approximately $1.3 million and $0.6 million, respectively.

The future minimum lease payments associated with the 26 Landsdowne Street lease as of September 30, 2023, are as follows (in thousands):

2023(1)	$	633
2024		2,572
2025		2,649
2026		2,729
2027		2,811
Thereafter		1,426
Total minimum lease payments		12,820
Less: imputed interest		(1,740)
Total lease liability	$	11,080

1. Amounts are for the three months ending December 31, 2023.

125 Sidney Street

In November 2021, the Company entered into a lease agreement comprising approximately 12,196 square feet of office space at 125 Sidney Street in Cambridge, Massachusetts, commencing November 2021. The Company began recognizing rent expense associated with this lease during November 2021. The lease ends on March 31, 2024. The Company has the option to extend the term of the lease for two successive one-year periods, at the market rate, by giving the landlord written notice of its election to exercise the extension at least nine months prior to the original expiration of the lease term. The lease has a total commitment of $1.7 million over the initial term, and includes escalating rent payments. Operating lease expense associated with this lease for the three and nine months ended September 30, 2023 was approximately $0.2 million and $0.5 million, respectively. No variable lease expense was recorded associated with this lease for the three and nine months ended September 30, 2023.

The future minimum lease payments associated with this lease as of September 30, 2023, are as follows (in thousands):

2023(1)	$	210
2024		210
Total minimum lease payments		420
Less: imputed interest		(5)
Total lease liability	$	415

1. Amounts are for the three months ending December 31, 2023.

13. Commitments and Contingencies

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 arising out of the relationship between such parties and the Company. In addition, the Company has entered into indemnification agreements with members of its board of directors and senior management 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 aware of any claims under indemnification arrangements, and it has not accrued any liabilities related to such obligations as of September 30, 2023 or December 31, 2022.

Legal Proceedings

On April 28, 2023, a class action complaint, *Celano v. Fulcrum Therapeutics, Inc., et al.*, Case No. 1:23-cv-11125-IT, was filed in the United States District Court for the District of New Jersey against the Company and current and former officers (the "Securities Action"). On May 19, 2023, the Securities Action was transferred to the United States District Court for the District of Massachusetts. On July 31, 2023, the court appointed a lead plaintiff, who filed an amended complaint on September 29, 2023. The Securities Action alleges violations of Section 10(b) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder against all defendants and control person violations of Section 20(a) against the individuals, related to the Company's February 2023 announcement that the U.S. Food and Drug Administration issued a clinical hold regarding the investigational new drug application for pociredir (formerly known as FTX-6058) for the potential treatment of sickle cell disease. The Securities Action alleges that the defendants made misleading statements and omitted to disclose material information related to the clinical hold and seeks, among other things, compensatory damages in connection with an allegedly inflated stock price between March 3, 2022, and March 8, 2023, as well as attorneys' fees and costs. The Company intends to defend vigorously against this litigation.

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 the costs related to its legal proceedings as they are incurred. No such costs have been incurred during the three and nine months ended September 30, 2023.

14. Defined Contribution Plan

The Company has a defined contribution savings plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants the option to elect to defer a portion of their annual compensation on a pretax basis. As currently established, the Company is not required to make contributions to the 401(k) Plan. The Company made $0.2 million and $0.6 million, respectively, in contributions to the 401(k) Plan for the three and nine months ended September 30, 2023. The Company made $0.2 million and $0.6 million, respectively, in contributions to the 401(k) Plan for the three and nine months ended September 30, 2022.

15. Net Loss per Share

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Outstanding stock options	10,108,766	5,929,065	10,108,766	5,929,065
Unvested restricted stock units	78,142	95,174	78,142	95,174
Total	10,186,908	6,024,239	10,186,908	6,024,239

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

The following discussion and analysis of our financial condition and results of operations should be read together with our consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and our Annual Report on Form 10-K filed with the Securities and Exchange Commission, or SEC, on March 9, 2023. 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, includes forward-looking statements that involve risks and uncertainties. As a result 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.

Overview

We are a clinical-stage biopharmaceutical company focused on developing small molecules to improve the lives of patients with genetically defined rare diseases in areas of high unmet medical need. Our most advanced clinical product candidate, losmapimod, is being developed for the potential treatment of FSHD. Our other clinical product candidate is pociredir, which is being developed for the potential treatment of certain hemoglobinopathies, including SCD. We initiated REACH, a randomized, double-blind, placebo-controlled, multi-national Phase 3 clinical trial of losmapimod in the second quarter of 2022 and we completed enrollment during September 2023. The trial enrolled 260 patients. We expect to report topline data in the fourth quarter of 2024.

In January 2023, we announced interim data from our Phase 1b clinical trial of pociredir in SCD. We completed enrollment in the 6 mg and 2 mg dose cohorts, and we do not plan to enroll additional subjects in these cohorts. Although we commenced enrollment in the 12 mg dose cohort, in February 2023, the FDA placed a full clinical hold on the Investigational New Drug (IND) application for pociredir for SCD, which was lifted in August 2023. The Phase 1b clinical trial is being re-initiated at the 12 mg once daily dose level, with that cohort expected to enroll approximately 10 patients, followed by an additional cohort of 10 patients at the 20 mg once a daily dose level. The protocol was amended to revise the inclusion and exclusion criteria to target patients with higher disease severity.

We have developed a proprietary technology that we employ to systematically identify and validate cellular drug targets that can potentially modulate gene expression to treat known root causes of genetically defined diseases. Our discovery approach led to the identification of both losmapimod for FSHD and pociredir for hemoglobinopathies, as well as a robust discovery pipeline. With our priorities focused on the development and potential commercialization of our two clinical-stage assets, losmapimod and pociredir, and ongoing work on our preclinical programs in hematology and muscle diseases, we are realigning our strategy and resources accordingly and will be winding down certain exploratory activities from our discovery efforts.

Since inception, our operations have focused on organizing and staffing our company, business planning, raising capital, establishing our intellectual property, building our discovery platform, including our proprietary compound library and technologies, identifying drug targets and potential product candidates, in-licensing assets, producing drug substance and drug product material for use in clinical trials and conducting preclinical studies and clinical trials. To date, we have funded our operations primarily from the sale of shares of our capital stock and from upfront payments received under our collaboration and license agreements.

We have incurred significant operating losses since our inception and we expect to continue to incur significant operating losses for the foreseeable future. Our ability to generate product revenue sufficient to achieve profitability, if ever, will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. Our net losses were $24.0 million and $72.6 million for the three and nine months ended September 30, 2023 and $23.7 million and $83.7 million for the three and nine months ended September 30, 2022, respectively. As of September 30, 2023, we had an accumulated deficit of $484.9 million. We expect our expenses and operating losses will increase substantially over the next several years in connection with our ongoing activities, as we:

- continue our clinical development of losmapimod and pociredir;
- continue our ongoing preclinical studies;
- advance clinical-stage product candidates into later stage trials such as REACH, the Phase 3 clinical trial of losmapimod for the treatment of FSHD;
- pursue the discovery of drug targets for other genetically-defined rare diseases and the subsequent development of any resulting product candidates, including for Diamond Blackfan Anemia under our recent license agreement with CAMP4;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- scale up our manufacturing processes and capabilities, or arrange for a third party to do so on our behalf, to support our clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval;

- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain regulatory approval;
- acquire or in-license products, product candidates, technologies and/or data referencing rights, such as our recent agreement with CAMP4;
- make any milestone payments to affiliates of GSK under our right of reference and license agreement with GSK upon the achievement of specified clinical or regulatory milestones, or to CAMP4 under our license agreement with CAMP4;
- maintain, expand, enforce, defend and protect our intellectual property;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts and our operations as a public company.

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 a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. 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, scale back or discontinue the development and commercialization of one or more of our product candidates, or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of increased expenses or the timing of 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 $257.1 million in cash, cash equivalents, and marketable securities. We believe that our existing cash, cash equivalents, and marketable securities as of September 30, 2023 will enable us to fund our operating expenses and capital expenditure requirements into 2026. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "—Liquidity and Capital Resources."

Components of Results of Operations

Revenue

We have not generated any revenue from product sales and do not expect to generate revenue from the sale of products for several years, if at all. If our development efforts for our current or future product candidates are successful and result in marketing approval, we may generate revenue in the future from product sales. We cannot predict if, when or to what extent we will generate revenue from the commercialization and sale of our product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates.

In December 2019, we entered into a collaboration and license agreement with Acceleron to identify biological targets to modulate specific pathways associated with a targeted indication within the pulmonary disease space. The agreement terminated effective October 1, 2022, following notification from Acceleron in June 2022 of its decision to terminate the agreement for convenience. For the three and nine months ended September 30, 2022, we recognized zero and $1.0 million, respectively of collaboration revenue under the Acceleron collaboration agreement. We did not recognize any collaboration revenue under the Acceleron collaboration agreement during the three and nine months ended September 30, 2023.

In July 2020, we entered into a collaboration and license agreement with MyoKardia, which we amended in April 2023, pursuant to which we granted to MyoKardia an exclusive worldwide license under certain intellectual property rights to research, develop, make, have made, use, have used, sell, have sold, offer for sale, have offered for sale, import, have imported, export, have exported, distribute, have distributed, market, have marketed, promote, have promoted, or otherwise exploit products directed against certain biological targets identified by us that are capable of modulating up to a certain number of genes of interest with relevance to certain genetically defined cardiomyopathies. MyoKardia was subsequently acquired by Bristol-Myers Squibb Company in November 2020. The primary goal of the collaboration is to identify and validate potential biological targets for further research, in order to support the development, manufacture and commercialization of product candidates by MyoKardia for the potential treatment of certain genetically defined cardiomyopathies.

Under the terms of the MyoKardia collaboration agreement, we received a $10.0 million upfront payment and a $2.5 million payment as prepaid research funding in July 2020. MyoKardia will also reimburse us for the costs of the research activities not covered by the prepaid research funding, up to a maximum amount of total research funding (including the prepaid research funding). Upon the achievement of specified preclinical, development and sales milestones, we will be entitled to preclinical milestone payments, development milestone payments and sales milestone payments of up to $298.5 million in the aggregate per target for certain potential cardiomyopathy gene targets, and of up to $150.0 million in the aggregate per target for certain other potential cardiomyopathy gene targets. To date, we have achieved a $2.5 million specified preclinical milestone. MyoKardia will also pay us tiered royalties ranging from a mid single-digit percentage to a low double-digit percentage based on MyoKardia's, and any of its affiliates' and sublicensees', annual worldwide net sales of products under the MyoKardia collaboration agreement directed against any identified target. The royalties are payable on a product-by-product basis during a specified royalty term, and may be reduced in specified circumstances.

For the three months ended September 30, 2023 and 2022, we recognized $0.8 million and $1.2 million, respectively, of collaboration revenue under the MyoKardia collaboration agreement. For the nine months ended September 30, 2023 and 2022, we recognized $1.9 million and $4.7 million, respectively, of collaboration revenue under the MyoKardia collaboration agreement. As of September 30, 2023 and December 31, 2022, we have recorded $0.3 million and $0.9 million, respectively, of deferred revenue associated with the MyoKardia collaboration agreement, which is classified as either current or noncurrent, net of current portion in our consolidated balance sheets based on the period over which the revenue is expected to be recognized. As of September 30, 2023, we had received $6.6 million of cost reimbursement payments and $2.5 million of milestone payments under the MyoKardia collaboration agreement. As of September 30, 2023, we recorded unbilled accounts receivable of $0.6 million related to reimbursable research and development costs under the MyoKardia collaboration agreement for activities performed during the three months ended September 30, 2023. As of September 30, 2023, we recorded no accounts receivable under the MyoKardia collaboration agreement.

In the future, we will recognize additional revenue associated with the $10.0 million upfront payment and the $2.5 million preclinical milestone achieved in December 2021 as we satisfy our performance obligation, and from reimbursement of costs incurred under the MyoKardia collaboration agreement. In the future, we may also generate additional revenue from milestones and royalty payments under the MyoKardia collaboration agreement. We expect that our revenue will fluctuate from quarter-to-quarter and year-to-year based upon our pattern of performance under the MyoKardia collaboration agreement and as a result of the timing, amount, and achievement of milestones and reimbursement of costs incurred under the MyoKardia collaboration agreement.

We may also in the future enter into additional license or collaboration agreements for our product candidates or intellectual property, and we may generate revenue in the future from payments as a result of such license or collaboration agreements.

Operating Expenses

Research and Development Expenses

Research and development expenses represent costs incurred by us for the discovery, development, and manufacture of our product candidates and include:

- external research and development expenses incurred under agreements with contract research organizations, contract manufacturing organizations, and consultants;
- salaries, payroll taxes, employee benefits and stock-based compensation expenses for individuals involved in research and development efforts;
- laboratory supplies;
- costs related to compliance with regulatory requirements;
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent, maintenance of facilities, insurance and other operating costs; and
- milestone expenses associated with our right of reference and license agreement with GlaxoSmithKline plc, or GSK.

We expense research and development costs as incurred. We recognize expenses for certain development activities, such as clinical trials and manufacturing, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment or other information provided to us by our vendors. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of expenses incurred. Non-refundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. These 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.

External costs represent a significant portion of our research and development expenses, which we track on a program-by-program basis following the nomination of a development candidate. Our internal research and development expenses consist primarily of personnel-related expenses, including stock-based compensation expense. We do not track our internal research and development expenses on a program-by-program basis as the resources are deployed across multiple projects.

The following table summarizes our external research and development expenses by program following nomination as a development candidate for the three and nine months ended September 30, 2023 and 2022. Pre-development candidate expenses, unallocated expenses and internal research and development expenses are classified separately. Losmapimod external expenses during the nine months ended September 30, 2022 includes a $5.0 million milestone achieved under our right of reference and license agreement with GSK upon the initiation of the REACH trial during the second quarter of 2022.

	Three Months Ended September 30,		Nine Months Ended September 30,	
(in thousands)	**2023**	**2022**	**2023**	**2022**
Losmapimod external expenses	$ 7,727	$ 4,497	$ 21,452	$ 17,941
Pociredir external expenses	1,110	2,923	5,665	12,114
Pre-development candidate expenses and unallocated expenses	4,196	3,597	10,636	12,281
Internal research and development expenses	5,205	4,349	15,049	15,880
Total research and development expenses	$ 18,238	$ 15,366	$ 52,802	$ 58,216

The successful development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing, and estimated costs of the efforts that will be necessary to complete the remainder of the development of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from our product candidates, if approved. This is due to the numerous risks and uncertainties associated with developing our product candidates, including the uncertainty related to:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to raise additional funds necessary to complete clinical development of and commercialize our product candidates;
- our ability to maintain our current research and development programs and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the progress of the development efforts of parties with whom we may enter into 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 raw materials and active pharmaceutical ingredient, or API, for use in production of our product candidates;
- our ability to establish and operate a manufacturing facility, or secure manufacturing supply through relationships with third parties;
- our ability to consistently manufacture our product candidates in quantities sufficient for use in clinical trials;
- our ability to obtain and maintain intellectual property protection and regulatory exclusivity, both in the United States and internationally;

- our ability to maintain, enforce, defend and protect our rights in our intellectual property portfolio;
- the commercialization of our product candidates, if and when approved;
- our ability to obtain and maintain third-party coverage and adequate reimbursement for our product candidates, if approved;
- the acceptance of our product candidates, if approved, by patients, the medical community and third-party payors;
- competition with other products; and
- a continued acceptable safety profile of our products following receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs and timing associated with the development of that product candidate, and potentially other candidates.

Research and development activities account for a significant portion of our operating expenses. We expect our research and development expenses to increase significantly in future periods as we continue to implement our business strategy, which includes advancing losmapimod for the treatment of FSHD, advancing pociredir for the treatment of certain hemoglobinopathies, including SCD, expanding our research and development efforts, including hiring additional personnel to support our research and development efforts, and seeking regulatory approvals for our product candidates that successfully complete clinical trials. In addition, product candidates in later stages of clinical development generally incur higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. As a result, we expect our research and development expenses to increase as our product candidates advance into later stages of clinical development. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development.

General and Administrative Expenses

General and administrative expenses consist of personnel-related costs, including salaries, benefits and stock-based compensation expense, for our personnel in executive, finance and accounting, human resources, business operations and other administrative functions, legal fees related to patent, intellectual property and corporate matters, fees paid for accounting and tax services, consulting fees and facility-related costs not otherwise included in research and development expenses.

We expect our general and administrative expenses will increase for the foreseeable future to support our expanded infrastructure and increased costs of expanding our operations and operating as a public company. These increases will likely include increased expenses related to accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs associated with operating as a public company.

Other Income, Net

Other income, net consists primarily of interest income related to our investments in cash equivalents and marketable securities.

Results of Operations

Comparison of the Three Months ended September 30, 2023 and 2022

The following summarizes our results of operations for the three months ended September 30, 2023 and 2022 along with the changes in those items in dollars:

(in thousands)	Three Months Ended September 30, 2023	Three Months Ended September 30, 2022	Change $
Collaboration revenue	$ 759	$ 1,183	$ (424)
Operating expenses:			
Research and development	18,238	15,366	2,872
General and administrative	9,961	9,707	254
Restructuring expenses	—	465	(465)
Total operating expenses	28,199	25,538	2,661
Loss from operations	(27,440)	(24,355)	(3,085)
Other income, net	3,423	617	2,806
Net loss	$ (24,017)	$ (23,738)	$ (279)

Collaboration Revenue

Collaboration revenue decreased by $0.4 million from $1.2 million for the three months ended September 30, 2022 to $0.8 million for the three months ended September 30, 2023. We recognize revenue under each of the Acceleron and MyoKardia collaboration agreements based on our pattern of performance related to the respective identified performance obligation, which is the period over which we will perform research services under each of the agreements. For the three months ended September 30, 2023 and 2022, we recognized no collaboration revenue under the Acceleron collaboration agreement and $0.8 million and $1.2 million, respectively, of collaboration revenue under the MyoKardia collaboration agreement. The Acceleron collaboration agreement terminated effective October 1, 2022.

Research and Development Expenses

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

(in thousands)	Three Months Ended September 30, 2023	Three Months Ended September 30, 2022	Change $
External research and development	$ 10,440	$ 8,457	$ 1,983
Employee compensation	5,205	4,349	856
Laboratory supplies	901	845	56
Facility costs	1,329	1,363	(34)
Other	363	352	11
Total research and development expenses	$ 18,238	$ 15,366	$ 2,872

Research and development expense increased by $2.9 million from $15.4 million for the three months ended September 30, 2022 to $18.2 million for the three months ended September 30, 2023. The increase in research and development expense was primarily attributable to the following:

- $2.0 million of increased external research and development costs, primarily due to the advancement of REACH as we completed enrollment in September 2023, partially offset by decreased costs for pociredir as a result of the clinical hold, which was lifted in August 2023; and
- $0.9 million of increased employee compensation costs, including a $0.2 million increase in stock-based compensation expense.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for the three months ended September 30, 2023 and 2022:

(in thousands)	Three Months Ended September 30, 2023	Three Months Ended September 30, 2022	Change $
Employee compensation	$ 6,111	$ 6,242	$ (131)
Professional services	2,379	2,298	81
Facility costs	640	569	71
Other	831	598	233
Total general and administrative expenses	$ 9,961	$ 9,707	$ 254

General and administrative expenses increased by $0.3 million from $9.7 million for the three months ended September 30, 2022 to $10.0 million for the three months ended September 30, 2023. The increase in general and administrative expenses was primarily attributable to the following:

- $0.2 million of increased other costs, including increased software costs;
- partially offset by $0.1 million of decreased employee compensation costs due to decreased headcount.

Other Income, Net

Other income, net increased by $2.8 million from $0.6 million for the three months ended September 30, 2022 to $3.4 million for the three months ended September 30, 2023. The increase was primarily attributable to an increased rate of return on our cash, cash equivalents, and marketable securities and an increase in our average cash and investment balance.

Comparison of the Nine Months ended September 30, 2023 and 2022

The following summarizes our results of operations for the nine months ended September 30, 2023 and 2022 along with the changes in those items in dollars:

(in thousands)	Nine Months Ended September 30, 2023	Nine Months Ended September 30, 2022	Change $
Collaboration revenue	$ 1,934	$ 5,657	$ (3,723)
Operating expenses:			
Research and development	52,802	58,216	(5,414)
General and administrative	31,804	31,564	240
Restructuring expenses	—	465	(465)
Total operating expenses	84,606	90,245	(5,639)
Loss from operations	(82,672)	(84,588)	1,916
Other income, net	10,093	852	9,241
Net loss	$ (72,579)	$ (83,736)	$ 11,157

Collaboration Revenue

Collaboration revenue decreased by $3.7 million from $5.7 million for the nine months ended September 30, 2022 to $1.9 million for the nine months ended September 30, 2023. We recognize revenue under each of the Acceleron and MyoKardia collaboration agreements based on our pattern of performance related to the respective identified performance obligation, which is the period over which we will perform research services under each of the agreements. For the nine months ended September 30, 2023 and 2022, we recognized zero and $1.0 million, respectively, of collaboration revenue under the Acceleron collaboration agreement and $1.9 million and $4.7 million, respectively, of collaboration revenue under the MyoKardia collaboration agreement. The Acceleron collaboration agreement terminated effective October 1, 2022.

Research and Development Expenses

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

(in thousands)	Nine Months Ended September 30, 2023	Nine Months Ended September 30, 2022	Change $
External research and development	$ 30,343	$ 33,250	$ (2,907)
Employee compensation	15,049	15,880	(831)
Laboratory supplies	2,599	3,555	(956)
Facility costs	3,640	4,309	(669)
Other	1,171	1,222	(51)
Total research and development expenses	$ 52,802	$ 58,216	$ (5,414)

Research and development expense decreased by $5.4 million from $58.2 million for the nine months ended September 30, 2022 to $52.8 million for the nine months ended September 30, 2023. The decrease in research and development expense was primarily attributable to the following:

- $2.9 million of decreased external research and development costs, primarily associated with decreased costs for pociredir as a result of the clinical hold from February to August 2023, and achievement of a $5.0 million milestone due to GSK upon initiation of REACH in the second quarter of 2022, partially offset by increased costs associated with the advancement of REACH as we completed enrollment in September 2023;
- $1.0 million in decreased laboratory supplies costs;
- $0.8 million in decreased employee compensation costs due to decreased headcount; and
- $0.7 million in decreased facilities costs.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for the nine months ended September 30, 2023 and 2022:

(in thousands)	Nine Months Ended September 30, 2023	Nine Months Ended September 30, 2022	Change $
Employee compensation	$ 19,088	$ 17,758	$ 1,330
Professional services	8,334	10,344	(2,010)
Facility costs	1,913	1,536	377
Other	2,469	1,926	543
Total general and administrative expenses	$ 31,804	$ 31,564	$ 240

General and administrative expenses increased by $0.2 million from $31.6 million for the nine months ended September 30, 2022 to $31.8 million for the nine months ended September 30, 2023. The increase in general and administrative expenses was primarily attributable to the following:

- $1.3 million of increased employee compensation costs, including a $1.4 million increase in stock-based compensation expense;
- $0.4 million of increased facility-related costs; and
- $0.5 million of increased other costs;
- partially offset by $2.0 million of decreased professional services costs, primarily due to decreased consulting and insurance costs.

Other Income, Net

Other income, net increased by $9.2 million from $0.9 million for the nine months ended September 30, 2022 to $10.1 million for the nine months ended September 30, 2023. The increase was primarily attributable to an increased rate of return on our cash, cash equivalents, and marketable securities and an increase in our average cash and investment balance.

Liquidity and Capital Resources

Sources of Liquidity

We have incurred significant operating losses since our inception and expect to continue to incur significant operating losses for the foreseeable future and may never become profitable. We have not yet commercialized any of our product candidates, which are in various phases of preclinical and clinical development, and we do not expect to generate revenue from sales of any products for several years, if at all. As of September 30, 2023, we have funded our operations primarily with aggregate gross proceeds of $712.5 million from the sale of shares of our capital stock and from upfront payments received under our collaboration and license agreements. As of September 30, 2023, we had cash, cash equivalents, and marketable securities of $257.1 million.

In January 2023, we completed a public offering of our common stock and issued and sold 9,615,384 shares of common stock at a public offering price of $13.00 per share, resulting in net proceeds of $117.3 million after deducting underwriting discounts and commissions and offering expenses.

Cash Flows

The following table provides information regarding our cash flows for the three months ended September 30, 2023 and 2022:

	Nine Months Ended September 30,	
(in thousands)	**2023**	**2022**
Net cash used in operating activities	$ (67,807)	$ (77,354)
Net cash (used in) provided by investing activities	(55,046)	48,775
Net cash provided by financing activities	117,835	84,105
Net (decrease) increase in cash, cash equivalents, and restricted cash	$ (5,018)	$ 55,526

Net Cash Used in Operating Activities

Net cash used in operating activities was $67.8 million during the nine months ended September 30, 2023 compared to $77.4 million during the nine months ended September 30, 2022. The decrease in net cash used in operating activities of $9.6 million was primarily due to a decrease in net loss, including as a result of decreased external research and development costs as a result of the clinical hold for pociredir, which was lifted in August 2023, and increased interest income.

Net Cash (Used in) Provided by Investing Activities

Net cash used in investing activities was $55.0 million during the nine months ended September 30, 2023 compared to net cash provided by investing activities of $48.8 million during the nine months ended September 30, 2022. The increase in net cash used in investing activities of $103.8 million was primarily due to net purchases of marketable securities during the nine months ended September 30, 2023, as compared to net maturities of marketable securities during the nine months ended September 30, 2022.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $117.8 million during the nine months ended September 30, 2023 compared to net cash provided by financing activities of $84.1 million during the nine months ended September 30, 2022. Net cash provided by financing activities during the nine months ended September 30, 2023 primarily consisted of net proceeds of $117.3 million from the January 2023 public offering of our common stock. Net cash provided by financing activities during the nine months ended September 30, 2022 primarily consisted of net proceeds of $80.8 million from the August 2022 completion of the public offering of our common stock.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing research and development activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, we expect to incur additional costs to support the growth of our organization. As a result, we expect to incur substantial operating losses and negative operating cash flows for the foreseeable future.

Based on our current operating plan, we believe that our existing cash, cash equivalents, and marketable securities as of September 30, 2023, will enable us to fund our operating expenses and capital expenditure requirements into 2026. However, we have based this estimate on assumptions that may prove to be wrong and we could exhaust our capital resources sooner than we expect.

Our funding requirements and timing and amount of our operating expenditures will depend largely on:

- the progress, costs and results of our clinical trials of losmapimod and pociredir;
- the scope, progress, costs and results of discovery research, preclinical development, laboratory testing and clinical trials for our current product candidates in additional indications or for any future product candidates that we may pursue, including under our recent license agreement with CAMP4;
- the number of and development requirements for other product candidates that we pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to enter into contract manufacturing arrangements for supply of API and manufacture of our product candidates and the terms of such arrangements;
- the success of our collaboration with MyoKardia;
- our ability to establish and maintain additional strategic collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the payment or receipt of milestones, royalties and other collaboration-based revenues, if any;
- the costs and timing of future commercialization activities, including product manufacturing, sales, marketing and distribution, for any of our product candidates for which we may receive marketing approval;
- the amount and timing of revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other products, product candidates, technologies or data referencing rights.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. We will need to continue to rely on additional financing to achieve our business objectives.

In addition to the variables described above, if and when any of our product candidates successfully complete development, we will incur substantial additional costs associated with regulatory filings, marketing approval, post-marketing requirements, maintaining our intellectual property rights, and regulatory protection, in addition to other commercial costs. We cannot reasonably estimate these costs at this time.

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, collaboration arrangements, strategic alliances and marketing, distribution or licensing arrangements. We currently have no credit facility or committed sources of capital. To the extent that we raise additional capital through the future sale of equity securities, the ownership interests of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through the issuance of debt securities, these securities could contain covenants that would restrict our operations. We may require additional capital beyond our currently anticipated amounts, and additional capital may not be available on reasonable terms, or at all. If we raise additional funds through collaboration arrangements, strategic alliances or marketing, distribution or licensing arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams 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 when needed, we may be required to delay, limit, reduce or terminate development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of these consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of expenses during the reporting periods. Our estimates are based on our historical experience, known trends and events, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities and amount of expense recognized that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We evaluate our estimates and assumptions on an ongoing basis. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates. During the three months ended September 30, 2023, there were no material changes to our critical accounting policies from those described in our Annual Report on Form 10-K filed with the SEC on March 9, 2023.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012 permits an “emerging growth company” such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected not to “opt out” of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either (i) irrevocably elect to “opt out” of such extended transition period or (ii) no longer qualify as an emerging growth company.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are a smaller reporting company, as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this item.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer (our principal executive officer) and our Chief Financial Officer (our principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2023. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of September 30, 2023, our Chief Executive Officer and our Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15(d)-15(f) under the Exchange Act) that occurred during the period covered by this Quarterly Report on Form 10-Q that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

On April 28, 2023, a class action complaint, *Celano v. Fulcrum Therapeutics, Inc., et al*., Case No. 1:23-cv-11125-IT, was filed in the United States District Court for the District of New Jersey against our company and current and former officers, or the Securities Action. On May 19, 2023, the Securities Action was transferred to the United States District Court for the District of Massachusetts. On July 31, 2023, the court appointed a lead plaintiff, who filed an amended complaint on September 29, 2023. The Securities Action alleges violations of Section 10(b) of the Exchange Act and Rule 10b-5 promulgated thereunder against all defendants and control person violations of Section 20(a) against the individuals, related to our February 2023 announcement that the FDA issued a clinical hold regarding the IND application for pociredir for the potential treatment of SCD. The Securities Action alleges that the defendants made misleading statements and omitted to disclose material information related to the clinical hold and seeks, among other things, compensatory damages in connection with an allegedly inflated stock price between March 3, 2022, and March 8, 2023, as well as attorneys' fees and costs. We intend to defend vigorously against this litigation.

Item 1A. Risk Factors.

Our future operating results could differ materially from the results described in this Quarterly Report on Form 10-Q due to the risks and uncertainties described below. You should consider carefully the following information about risks below in evaluating our business. If any of the following risks actually occur, our business, financial conditions, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline. In addition, we cannot assure investors that our assumptions and expectations will prove to be correct. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements. See "Cautionary Note Regarding Forward-Looking Statements" on page i of this Quarterly Report on Form 10-Q for a discussion of some of the forward-looking statements that are qualified by these risk factors. Factors that could cause or contribute to such differences include those factors discussed below.

Risks Related to our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $109.9 million for the year ended December 31, 2022 and $72.6 million for the nine months ended September 30, 2023. As of September 30, 2023, we had an accumulated deficit of $484.9 million. To date, we have funded our operations primarily from the sale of shares of our capital stock and from upfront payments received under our collaboration and license agreements. We have devoted substantially all of our financial resources and efforts to research and development, including clinical trials and preclinical studies. We are still in the early stages of development of our product candidates, and we have not completed development of any product candidates. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- continue our clinical development of losmapimod and pociredir;
- continue our ongoing preclinical studies;
- advance clinical-stage product candidates through later stage trials, such as REACH, the Phase 3 clinical trial of losmapimod for the treatment of FSHD;
- pursue the discovery of drug targets for other genetically-defined rare diseases and the subsequent development of any resulting product candidates, including for DBA under our recent license agreement with CAMP4;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- scale up our manufacturing processes and capabilities, or arrange for a third party to do so on our behalf, to support our clinical trials of our product candidates and commercialization of any of our product candidates for which we may obtain marketing approval;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain regulatory approval;
- acquire or in-license products, product candidates, technologies and/or data referencing rights , such as our recent agreement with CAMP4;

- make any milestone payments to affiliates of GSK, under our right of reference and license agreement with GSK upon the achievement of specified clinical or regulatory milestones, or to CAMP4 under our license agreement with CAMP4;
- maintain, expand, enforce, defend and protect our intellectual property;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts and our operations as a public company.

To become and remain profitable, we must succeed in developing, and eventually commercializing, a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses will increase if, among other things:

- we are required by the FDA, the EMA, or other regulatory authorities to perform trials or studies in addition to, or different than, those expected;
- there are any delays in completing our clinical trials or the development of any of our product candidates, such as the clinical hold imposed by the FDA on the pociredir IND, which was lifted in August 2023; or
- there are any third-party challenges to our intellectual property or we need to defend against any intellectual property-related claim.

Even 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 depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or even continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we continue our ongoing and planned clinical trials of losmapimod and pociredir, continue research and development and initiate additional clinical trials of, and seek regulatory approval for, these and other product candidates. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance our preclinical activities and clinical trials. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Given current uncertainty in the capital markets and other factors, such funding may not be available on terms favorable to us or at all. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

Our future capital requirements will depend on many factors, including:

- the progress, costs and results of our ongoing clinical trials of losmapimod, including REACH, the Phase 3 clinical trial of losmapimod for the treatment of FSHD, which completed enrollment in September 2023, and our Phase 1b clinical trial of pociredir in SCD;
- additional planned clinical trials;
- the scope, progress, costs and results of discovery research, preclinical development, laboratory testing and clinical trials for our current product candidates in additional indications or for any future product candidates that we may pursue;
- the number of and development requirements for other product candidates that we pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to enter into contract manufacturing arrangements for supply of active pharmaceutical ingredient, or API, and manufacture of our product candidates and the terms of such arrangements;
- the success of our collaboration with MyoKardia or under our recent license agreement with CAMP4;
- our ability to establish and maintain additional strategic collaborations, licensing or other arrangements and the financial terms of such arrangements;

- the payment or receipt of milestones, royalties and other collaboration-based revenues, if any;
- the costs and timing of future commercialization activities, including product manufacturing, sales, marketing and distribution, for any of our product candidates for which we may receive marketing approval;
- the amount and timing of revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other products, product candidates, technologies or data referencing rights.

As of September 30, 2023, we had cash, cash equivalents, and marketable securities of approximately $257.1 million. We believe that our cash, cash equivalents, and marketable securities as of September 30, 2023 will enable us to fund our operating expenses and capital expenditure requirements into 2026. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us. As a result, we could deplete our capital resources sooner than we currently expect.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Commercial revenues, if any, will not be derived unless and until we can achieve sales of products, which we do not anticipate for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all, and may become even more difficult to obtain due to rising interest rates and the current downturn in the U.S. capital markets and the biotechnology sector in general. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more of our product candidates or discovery stage programs or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates. We may also choose to further realign our operations to achieve additional operational efficiencies beyond the strategic realignment commenced in August 2022.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights as common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures or declaring dividends.

If we raise additional 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 when needed, we may be required to delay, limit, reduce or terminate 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.

We have in the past relied in part on sales of our common stock through an at-the-market, or ATM, offering program. Increased volatility and decreases in market prices of equity securities generally and of our common stock in particular may have an adverse impact on our willingness and/or ability to continue to sell our common stock through our ATM offering program. Decreases in these sales could affect the cost or availability of equity capital, which could in turn have an adverse effect on our business, including current operations, future growth, revenues, net income and the market prices of our common stock.

In May 2022, we established a new ATM offering program to sell shares of our common stock having an aggregate offering price of up to $50.0 million from time to time. In January 2023, immediately prior to commencing our underwritten public offering of common stock, we suspended our use of and terminated the prospectus supplement related to the ATM offering program. We may not make any sales of securities pursuant to the ATM offering program unless and until we file a new prospectus supplement. However, given the overall volatility in the capital markets, even if a new prospectus supplement is filed, we may not be willing or able to continue to raise equity capital through our ATM offering program. We may, therefore, need to turn to other sources of funding that may have terms that are not favorable to us, or reduce our business operations given capital constraints.

Alternative financing arrangements could involve issuances of one or more types of securities, including common stock, preferred stock, convertible debt, warrants to acquire common stock or other securities. These securities could be issued at or below the then prevailing market price for our common stock. In addition, if we issue debt securities, the holders of the debt would have a claim to our assets that would be superior to the rights of stockholders until the principal, accrued and unpaid interest and any premium or make-whole has been paid. In addition, if we borrow funds and/or issue debt securities through a subsidiary, the lenders and/or holders of those debt securities would have a right to payment that would be effectively senior to our equity ownership in the subsidiary, which would adversely affect the rights of holders of both our equity securities and, if any, our debt and debt securities.

Interest on any newly-issued debt securities and/or newly-incurred borrowings would increase our operating costs and reduce our net income, and these impacts may be material. If the issuance of new securities results in diminished rights to holders of our common stock, the market price of our common stock could be materially and adversely affected. Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences could result in a material adverse effect on our business, operating results, financial condition and prospects.

Our limited operating history may make it difficult for stockholders to evaluate the success of our business to date and to assess our future viability.

We commenced activities in 2015 and are a clinical-stage biotechnology company. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, establishing our intellectual property, building our discovery platform, identifying drug targets and potential product candidates, in-licensing assets, producing drug substance and drug product material for use in clinical trials and conducting preclinical studies and clinical trials. We have not yet demonstrated our ability to successfully develop any product candidate, obtain regulatory approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions stockholders make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

In addition, as our business grows, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Our business was negatively impacted by the COVID-19 pandemic and may in the future be impacted by any future pandemics. In addition, the effects of this pandemic may continue to, and any future pandemics may, adversely impact economies worldwide, which could result in adverse effects on our business and operations.

We experienced enrollment delays in our ReDUX4 clinical trial due to the COVID-19 pandemic as the clinical trial sites for our ReDUX4 clinical trial temporarily postponed trial-related activities. We also saw temporary disruptions in other business activities due to a temporary reduction in workforce presence at our Cambridge research facility, and COVID-19 had a significant impact on economies worldwide. Future pandemics may arise, and they, like COVID-19, could impact our company, our CMOs and contract research organizations, or CROs, creating disruptions that affect our ability to initiate and complete preclinical studies or clinical trials, disrupt our supply chain for our research and development activities, and disrupt any then planned or ongoing clinical trials for any number of reasons. Any future pandemics could similarly impact patient recruitment or retention for clinical trials, or result in resources being redirected in a way that adversely impacts our ability to progress regulatory approvals and protect our intellectual property. In addition, as with COVID-19 pandemic, we may face impediments to regulatory meetings and approvals due to recommended safety measures intended to limit in-person interactions in any future pandemic.

The COVID-19 pandemic caused significant disruptions in the financial markets and any future pandemic could similarly cause such disruptions, which could impact our ability to raise additional funds through public offerings and may also impact the volatility of our stock price and trading in our stock. We cannot be certain what the overall impact of any future pandemic will be on our business. The extent of the impact of COVID-19 and any future pandemic on our business, financial condition, results of operations and prospects will depend on future developments that are uncertain.

Changes in tax laws or in their implementation or interpretation may 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), including with respect to net operating losses and research and development tax credits, 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. For example, under Section 174 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, in taxable years beginning after December 31, 2021, expenses that are incurred for research and development in the United States will be capitalized and amortized, which may have an adverse effect on our cash flow. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

Our ability to use our net operating losses and research and development tax credit carryforwards to offset future taxable income may be subject to certain limitations.

As of December 31, 2022, we had federal and state net operating loss carryforwards of $275.1 million and $272.6 million, respectively, which begin to expire in 2036. Approximately $251.5 million of the federal net operating losses can be carried forward indefinitely. As of December 31, 2022, we also had federal orphan drug credits of $14.6 million, which begin to expire in 2040. As of December 31, 2022, we also had federal and state research and development tax credit carryforwards of $6.9 million and $4.0 million, respectively, which begin to expire in 2035 and 2030, respectively. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities.

In general, under Section 382 of the Code, and corresponding provisions of state law, a corporation that undergoes an “ownership change,” which is generally defined as a greater than 50% change, by value, in its equity ownership by certain stockholders over a three-year period, is subject to limitations on its ability to utilize its pre-change net operating losses and research and development tax credit carryforwards to offset future taxable income. We conducted an analysis under Section 382 of the Code to determine if historical changes in ownership through December 31, 2021 would limit or otherwise restrict our ability to utilize our pre-change net operating losses and research and development tax credit carryforwards to offset future taxable income. As a result of the analysis, we do not believe that there are any significant limitations on our ability to utilize our net operating losses and research and development tax credit carryforwards to offset future taxable income. However, we may experience such ownership changes in the future (which may be outside our control). As a result, if, and to the extent that, we earn net taxable income, our ability to use our pre-change net operating losses and research and development tax credit carryforwards to offset such taxable income may be subject to limitations. Our net operating losses or credits may also be impaired under state law.

We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future; thus, we do not know whether or when we will generate taxable income necessary to utilize our net operating losses or research and development tax credit carryforwards.

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 financial condition and results of operations.

Events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. In March 2023, a number of banks (e.g., Silicon Valley Bank, Signature Bank and Silvergate Capital Corp.) were placed into receivership, followed by First Republic Bank in May 2023. Although the Federal Deposit Insurance Corporation, or FDIC, and others have taken steps to reduce risk to uninsured depositors, borrowers under credit agreements, letters of credit and certain other financial instruments with such banks or any other financial institution that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder. Even though 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 affecting the financial services industry or economy in general, such as these recent bank failures. These factors could also include, among others, 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 and the supervision thereof. In addition, investor concerns regarding the United States 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 contractual obligations or result in violations of federal or state wage and hour laws, which could have material adverse effect on our liquidity and on our business, financial condition or results of operations.

Risks Related to the Discovery and Development of our Product Candidates

We are early in our development efforts, and we only have two clinical-stage product candidates. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts, and we have advanced only two product candidates into clinical trials, losmapimod for the treatment of FSHD, and pociredir for the treatment of SCD (which was on clinical hold between February and August 2023). We have invested substantially all of our efforts and financial resources in identifying and validating and conducting clinical trials on cellular drug targets that can potentially modulate gene expression to address the root cause of genetically-defined rare diseases. Our ability to generate product revenues, which we do not expect will occur for several years, if ever, will depend heavily on the successful development, regulatory approval and eventual commercialization of our product candidates. The success of our product candidates will depend on several factors, including the following:

- successfully completing preclinical studies and clinical trials;
- allowance by the FDA or other regulatory agencies of the INDs, clinical trial applications, or CTAs, or other regulatory filings for losmapimod, pociredir and future product candidates;
- expanding and maintaining a workforce of experienced scientists and others to continue to develop our product candidates;
- applying for and receiving marketing approvals from applicable regulatory authorities;
- obtaining and maintaining intellectual property protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- establishing sales, marketing and distribution capabilities and successfully launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;
- acceptance of the products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining coverage, adequate pricing and adequate reimbursement from third-party payors, including government payors;
- maintaining, enforcing, defending and protecting our rights in our intellectual property portfolio;
- not infringing, misappropriating or otherwise violating others' intellectual property or proprietary rights; and
- maintaining a continued acceptable safety profile of the products following receipt of any regulatory approvals.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully develop and commercialize our product candidates, which would materially harm our business.

We may not be successful in our efforts to build a pipeline of product candidates.

Our current strategy is focused on developing small molecules to improve the lives of patients with genetically defined rare diseases. Even if we are successful in identifying drug targets and potential product candidates, such candidates that we identify may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance. Identifying, developing, obtaining regulatory approval for and commercializing additional product candidates will require substantial additional funding and is prone to the risks of failure inherent in product development. We cannot provide stockholders any assurance that we will be able to successfully identify additional product candidates, including as a result of our collaboration with MyoKardia, advance any additional product candidates through the development process or successfully commercialize any such additional product candidates. Regulatory authorities have substantial discretion in the approval process and may cause delays in the approval or rejection of an application. As a result of these factors, it is difficult for us to predict the time and cost of product candidate development. There can be no assurance that any development problems we experience in the future related to our discovery technologies or any of our research or development programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. If we do not successfully identify, develop, obtain regulatory approval for and commercialize product candidates, we will not be able to generate product revenues.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. The results of preclinical studies and early clinical trials may not be predictive of future results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We have two product candidates in clinical development. The risk of failure for each of our product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. We have not yet completed a pivotal clinical trial of any product candidate. Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses. For example, pociredir, our clinical trial stage candidate to treat SCD, is an embryonic ectoderm development, or EED, inhibitor. EED is a member of the PRC2 complex, which also includes EZH2. There are approved products in the EZH2 class of medications and their approved labeling outlines safety risks, including an increased risk of malignancies. In the event that pociredir has similar safety risks as other PRC2 medications, this could impact its acceptance. Even if the clinical trials are successful, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application.

Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our planned INDs and other regulatory filings in the United States and abroad. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or other regulatory agencies will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our current or future product candidates. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin or continue. For example, in February 2023, the FDA imposed a clinical hold on our IND for pociredir in SCD. We worked diligently to resolve the hold as soon as possible, and in August 2023, the FDA lifted the clinical hold. Product candidates are subject to continued preclinical safety studies, which may be conducted concurrent with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future clinical trials and could impact our ability to continue to conduct our clinical trials.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, or at all. For example, we revised the inclusion and exclusion criteria of our clinical trial of pociredir in SCD to address the clinical hold imposed by the FDA, and there can be no certainty as to whether we will be successful in completing the clinical trial with its revised design. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, but not limited to, flaws in study design, dose selection issues, placebo effects, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and preliminary or interim results of a clinical trial do not necessarily predict final results. For example, our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials. A lack of clinical benefit may be due to insufficient dosing or for other reasons. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Furthermore, the failure of any of our product candidates to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of our other product candidates and/or cause the FDA or other regulatory authorities to require additional testing before approving any of our product candidates.

As described in Item 1 “Business—Licenses and Collaborations--Right of Reference and License Agreement with GlaxoSmithKline” in our Annual Report on Form 10-K for the year ended December 31, 2022, or the 2022 Annual Report, we have entered into a right of reference and license agreement, as amended, with affiliates of GSK. Although losmapimod was originally evaluated by GSK in nearly 3,600 subjects, GSK did not evaluate losmapimod in FSHD or in any other muscular dystrophy, and most of the subjects in these trials were given a dose that was lower than our planned dosage of 15 mg of losmapimod twice per day. Accordingly, the safety data generated from GSK’s clinical trials of losmapimod may not be predictive or indicative of the results of our clinical trials. Similarly, while we believe the safety data from GSK’s clinical trials may, in part, support the safety database for losmapimod, GSK evaluated a limited number of subjects at a dose of 15 mg twice daily.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards, or IRBs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- regulators may decide the design of our clinical trials is flawed, for example if our trial protocol does not evaluate treatment effects in trial subjects for a sufficient length of time;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- we may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, or, if we seek accelerated approval, biomarker efficacy endpoints that applicable regulatory authorities would consider likely to predict clinical benefit;
- preclinical testing may produce results based on which we may decide, or regulators may require us, to conduct additional preclinical studies before we proceed with certain clinical trials, limit the scope of our clinical trials, halt ongoing clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may decide, or regulators or IRBs may require us, to suspend or terminate clinical trials of our product candidates for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- regulators or IRBs may require us to perform additional or unanticipated clinical trials to obtain approval or we may be subject to additional post-marketing testing requirements to maintain regulatory approval;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs to suspend or terminate the trials;
- unforeseen global instability, including political instability, such as the Russian invasion of Ukraine or recent hostilities in Israel and Gaza Strip, or instability from an outbreak of pandemic or contagious disease in or around the countries in which we conduct our clinical trials, could delay the commencement or rate of completion of our clinical trials; and
- regulators may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a risk evaluation and mitigation strategy, or REMS.

For example, in response to the COVID-19 pandemic, the clinical trial sites for our ReDUX4 trial temporarily postponed trial-related activities, impacting our clinical trial execution plans, and we cannot be certain that we will not face other postponements or similar difficulties in the future. Further, in February 2023, the FDA imposed a clinical hold on our IND for pociredir in SCD, which halted our clinical trial until the FDA lifted the clinical hold in August 2023.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;

- obtain approval with labeling or a REMS that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. We may also determine to change the design or protocol of one or more of our clinical trials, including to add additional patients or arms, which could result in increased costs and expenses and/or delays. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Because we are developing some of our product candidates for the treatment of diseases in which there is limited clinical experience and, in some cases, using new endpoints or methodologies, the FDA or other regulatory authorities may not consider the endpoints of our clinical trials to predict or provide clinically meaningful results.

There are currently no therapies approved to treat FSHD, and there may be no therapies approved to treat the underlying causes of diseases that we attempt to address or may address in the future. As a result, the design and conduct of a clinical trial or trials of the product candidates for the treatment of these diseases may take longer, be more costly or be less effective as part of the novelty of development in these diseases. In some cases, we may use new or novel endpoints or methodologies, such as RWS, which has not been proven for registration to our knowledge. The FDA and other regulatory authorities have indicated support for RWS as a primary endpoint with additional and appropriate supportive data from secondary endpoints. However, such regulatory authorities may not consider the endpoints of our clinical trial(s) to provide clinically meaningful results, even where we believe such results are clinically meaningful. For example, while we have met with regulators to discuss the REACH trial design and registration strategy for losmapimod for FSHD, including our proposed endpoints for REACH, regulators may require additional data to support the RWS functional primary endpoint for approval of losmapimod for FSHD.

Even if the FDA does find our primary endpoint to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoint to a magnitude, duration or degree of statistical significance in any pivotal or other clinical trials we may conduct for our product candidates. Even if we do meet the primary endpoint, our trials may produce results that are unpredictable or inconsistent with the results of the other, more traditional efficacy endpoints in the trials. The FDA also could ascribe substantial weight to other efficacy endpoints when interpreting the clinical trial data, such that even if we achieve statistically significant results on our primary endpoint, the FDA may regard the failure to show a statistically significant effect on our secondary efficacy endpoints as raising questions about the efficacy of the drug. The FDA also weighs the benefits of a product against its risks and the FDA may view the efficacy results in the context of safety as not being supportive of approval. Other regulatory authorities in Europe and other countries may make similar findings with respect to these endpoints.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Identifying and qualifying patients to participate in and complete clinical trials for our product candidates is critical to our success. Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients who remain in the trial until its conclusion. For example, in our Phase 1b trial of pociredir, although we enrolled six subjects in the initial cohort, only three subjects remained evaluable as of the initial data cutoff date. Subsequently, we modified the study protocol to monitor subject adherence. However, if such protocols do not improve adherence and improve compliance, we may not be able to generate meaningful data. Furthermore, we may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. We revised the design of our clinical trial of pociredir in SCD to address the clinical hold imposed by the FDA, and there can be no certainty as to whether we will be successful in completing the clinical trial with its revised design, which include updated inclusion and exclusion criteria and thus a narrower set of eligible patients. Because of our primary focus on genetically-defined rare diseases, we may have difficulty enrolling a sufficient number of eligible patients.

Patient enrollment is affected by a variety of other factors, including:

- the prevalence and severity of the disease under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidate under trial;

- the requirements of the trial protocols, including invasive procedures such as muscle biopsies or medical resonance imaging (MRI), which requires the use of specialized equipment;
- the availability of existing treatments for the indications for which we are conducting clinical trials;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients;
- the conduct of clinical trials by competitors for product candidates that treat the same indications as our product candidates;
- the ability to identify specific patient populations for biomarker-defined trial cohort(s); and
- the cost to, or lack of adequate compensation for, prospective patients.

Our inability to locate and enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

If serious adverse events or unacceptable side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.

If our product candidates are associated with serious adverse events or undesirable side effects in clinical trials or have characteristics that are unexpected in clinical trials or preclinical testing, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

For example, in February 2023, the FDA placed our IND for pociredir on clinical hold based on hematological malignancies observed in nonclinical toxicology studies. We addressed the FDA’s concern as diligently as possible, including FDA’s request for information about an SCD patient population with an appropriate benefit-risk profile for further clinical development of pociredir, and FDA's request for information to define the potential risk in any further studies that may be conducted in healthy volunteers. Although the FDA lifted the clinical hold in August 2023, we cannot make assurances that patients treated with pociredir will not develop hematological malignancies or other adverse events in the future. We also cannot make assurances that additional observations in preclinical studies of hematological malignancies or other adverse events will not occur. If such additional adverse events were to emerge, further advancement of our clinical studies could be halted or delayed and we may not receive regulatory approval for pociredir. Even if we receive regulatory approval for pociredir, our labeling may be restricted and/or market acceptance for our product may be diminished, and the commercial potential of our pociredir program may be materially and negatively impacted.

In pharmaceutical development, many compounds that initially show promise in early-stage or clinical testing are later found to cause side effects that delay or prevent further development of the compound.

Additionally, if results of our clinical trials reveal unacceptable side effects, we, the FDA or the IRBs at the institutions in which our studies are conducted could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete any of our clinical trials. If we elect or are forced to suspend or terminate any clinical trial of our product candidates, the commercial prospects of such product candidate will be harmed, and our ability to generate product revenue from such product candidate will be delayed or eliminated. Any of these occurrences could materially harm our business.

If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the drug could be compromised.

Clinical trials of our product candidates are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If one or more of our product candidates receives regulatory approval, and we, or others, later discover that they are less effective than previously believed, or cause undesirable side effects, a number of potentially significant negative consequences could result, including:

- withdrawal or limitation by regulatory authorities of approvals of such product;
- seizure of the product by regulatory authorities;
- recall of the product;
- restrictions on the marketing of the product or the manufacturing process for any component thereof;
- requirement by regulatory authorities of additional warnings on the label, such as a “black box” warning or contraindication;
- requirement that we implement a REMS or create a medication guide outlining the risks of such side effects for distribution to patients;
- commitment to expensive post-marketing studies as a prerequisite of approval by regulatory authorities of such product;
- the product may become less competitive;
- initiation of regulatory investigations and government enforcement actions;
- initiation of legal action against us to hold us liable for harm caused to patients; and
- harm to our reputation and resulting harm to physician or patient acceptance of our products.

Any of these events could prevent us from achieving or maintaining market acceptance of a particular product candidate, if approved, and could significantly harm our business, financial condition, and results of operations.

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

Because we have limited financial and managerial resources, we are focusing our research and development efforts on rare neuromuscular, muscular, hematologic and central nervous system disorders. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Failure to allocate resources or capitalize on strategies in a successful manner will have an adverse impact on our business.

We are conducting clinical trials of losmapimod in patients with FSHD in Europe, the United Kingdom, and Canada and currently plan to conduct additional clinical trials for our product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations.

We are currently conducting a Phase 3 clinical trial, an open label extension of our Phase 2b clinical trial, and an open label extension of our Phase 2 open label clinical trial of losmapimod in patients with FSHD in Europe, the United Kingdom, and Canada. We may also conduct additional clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and be performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations, including good clinical practices, and FDA’s ability to validate the data. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates.

Risks Related to the Commercialization of our Product Candidates

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, and the market opportunity for any of our product candidates, if approved, may be smaller than we estimate.

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages of our product candidates compared to the advantages and relative risks of alternative treatments;
- the effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to offer our products, if approved, for sale at competitive prices;
- the clinical indications for which the product is approved;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement, and patients' willingness to pay out of pocket for required co-payments or in the absence of third-party coverage or adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products, if approved, together with other medications.

Our assessment of the potential market opportunity for our product candidates is based on industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties, one of which we commissioned. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications and third-party research, surveys and studies, which may be based on a small sample size and fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. If any of our assumptions or estimates, or these publications, research, surveys or studies prove to be inaccurate, then the actual market for any of our product candidates may be smaller than we expect, and as a result our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

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

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales, marketing and distribution organization, either ourselves or through collaborations or other arrangements with third parties.

In the future, we expect to build a focused, specialty sales and marketing infrastructure to market some of our product candidates in the United States, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force 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 capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales, marketing, coverage or reimbursement, customer service, medical affairs and other support personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and we enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are acceptable to us. We likely will 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. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of many of the disease indications for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

For example, we are aware of several product candidates in clinical development that could be competitive with product candidates that we may successfully develop and commercialize. See Item 1 “Business — Competition” in the 2022 Annual Report.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

If the market opportunities for our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because certain of the target patient populations of our product candidates are small, and the addressable patient population even smaller, we must be able to successfully identify patients and capture a significant market share to achieve profitability and growth.

We primarily focus our research and product development on treatments for genetically-defined rare diseases. Given the small number of patients who have the rare diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research that we conducted, and may prove to be incorrect or contain errors. New studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations for many of the indications we are evaluating are very small, we may never achieve profitability despite obtaining such significant market share.

The target patient populations for some of the indications we are evaluating are relatively small, and there is currently no standard of care treatment directed at some of our target indications, such as FSHD. As a result, the pricing and reimbursement of our product candidates, if approved, is uncertain, but must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be adversely affected.

We rely, and expect to continue to rely, on CMOs to manufacture our product candidates. If we are unable to enter into such arrangements as expected or if such organizations do not meet our supply requirements, development and/or commercialization of our product candidates may be delayed.

We do not have any manufacturing facilities and rely, and expect to continue to rely, on third parties to manufacture clinical supplies of our product candidates and we expect to rely on third parties to manufacture commercial supplies of our products, if and when approved for marketing by applicable regulatory authorities, as well as for packaging, sterilization, storage, distribution and other production logistics. If we are unable to enter into such arrangements on the terms or timeline we expect, development and/or commercialization of our product candidates may be delayed.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or manufacture our product candidates in accordance with regulatory requirements, if there are disagreements between us and such parties or if such parties are unable to expand capacities to support commercialization of any of our product candidates for which we obtain marketing approval, we may not be able to fulfill, or may be delayed in producing sufficient product candidates to meet, our supply requirements, or 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 manufacturer, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trial supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original manufacturer 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 manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. 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 the FDA or another regulatory authority. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a manufacturer may possess technology related to the manufacture of our product candidate that such manufacturer owns independently. This would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another manufacturer manufacture our product candidates. In addition, 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. These facilities may also be affected by natural disasters, such as floods or fire, as well as public health issues (for example, an outbreak of a contagious disease such as COVID-19), or such facilities could face manufacturing issues, such as contamination or regulatory concerns following a regulatory inspection of such facility.

Our third-party manufacturers will be subject to inspection and approval by the FDA before we can commence the manufacture and sale of any of our product candidates, and thereafter subject to FDA inspection from time to time. Failure by our third-party manufacturers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidates may result in regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses.

We or our third-party manufacturers may also encounter shortages in the raw materials or API necessary to produce our product candidates in the quantities needed for our clinical trials or, if our product candidates are approved, in sufficient quantities for commercialization or to meet an increase in demand, as a result of capacity constraints or delays or disruptions in the market for the raw materials or API, including shortages caused by the purchase of such raw materials or API by our competitors or others. The failure of us or our third-party manufacturers to obtain the raw materials or API necessary to manufacture sufficient quantities of our product candidates, may have a material adverse effect on our business.

Our reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities. Although we believe we have obtained sufficient losmapimod tablets from GSK to complete our ongoing clinical trials of losmapimod for the treatment of FSHD, we cannot be sure we have correctly estimated our drug product and API requirements or that such drug product or API will not expire before we want to use it. We have also engaged CMOs to prepare our own API and to manufacture losmapimod tablets. Although we believe we have produced sufficient losmapimod tablets to complete our planned Phase 3 registrational trial, we cannot be sure we have correctly estimated our drug product and API requirements or that such drug product or API will not expire before we want to use it. In addition, although we believe we have obtained sufficient quantities of pociredir from a CMO for the completion of our Phase 1b clinical trial for SCD, we cannot be sure we have correctly estimated our drug product requirements, which could delay, prevent or impair our development efforts.

We expect to rely on third parties for the manufacture of pociredir for any future clinical trials and for the manufacture of any future product candidates for preclinical and clinical testing. We also expect to rely on third-party manufacturers or third-party collaborators for the manufacture of commercial supply of any other product candidates for which we or our collaborators obtain marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

Our product candidates and any products 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 or a source for bulk drug substance. If any of our future contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our 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 our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

The regulations that govern marketing approvals, pricing, coverage 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 our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval. See Item 1 “Business — Government Regulation and Product Approval — Pharmaceutical Insurance Coverage and Health Care Reform” in the 2022 Annual Report.

Our ability to commercialize any product candidates 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 government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and 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. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate 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 we obtain marketing approval. 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.

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 similar regulatory authorities outside of the United States. 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 expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. 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. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private 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.

There can be no assurance that our product candidates, even if they are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors, or that coverage and an adequate level of reimbursement will be available or that third-party payors’ reimbursement policies will not adversely affect our ability to sell our product candidates profitably.

Our future growth depends, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties that, if they materialize, could harm our business.

Our future profitability will depend, in part, on our ability to commercialize our product candidates in markets outside of the United States and the European Union. If we commercialize our product candidates in foreign markets, we will be subject to additional risks and uncertainties, including:

- economic weakness, including inflation, or political instability in particular economies and markets, which could include localized disputes that have a broader regional or global impact (such as the Russian invasion of Ukraine or recent hostilities in Israel and Gaza Strip);
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, many of which vary between countries;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- tariffs and trade barriers, as well as other governmental controls and trade restrictions;
- other trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or foreign governments;
- longer accounts receivable collection times;
- longer lead times for shipping;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is common;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries, and related prevalence of generic alternatives to therapeutics;
- foreign currency exchange rate fluctuations and currency controls;
- differing foreign reimbursement landscapes;
- uncertain and potentially inadequate reimbursement of our products; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

If risks related to any of these uncertainties materializes, it could have a material adverse effect on our business.

Clinical trial and product liability lawsuits against us could divert our resources and could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of clinical trial and product liability exposure related to the testing of our product candidates in human clinical trials, and we will face an even greater risk if we commercially sell any products that we may develop. While we currently have no products that have been approved for commercial sale, the current and future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will 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;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We currently hold $10 million in clinical trial liability insurance coverage in the aggregate, with a per incident limit of $10 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. 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. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Risks Related to our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, which may harm our business.

We currently rely on third-party contract CROs to conduct our clinical trials. We plan to rely on third-party CROs or third-party research collaboratives to conduct any future clinical trials. We do not plan to independently conduct clinical trials of our other product candidates. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. These agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities might be delayed.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize our product candidates. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors.

We also rely, and expect to continue to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We have entered into, and may in the future enter into, collaborations with third parties for the discovery, development or commercialization of our product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates and our business could be adversely affected.

We have a collaboration and license agreement with MyoKardia (for certain genetically defined cardiomyopathies). See Item 1 “Business—License Agreements and Collaborations” in the 2022 Annual Report. While we have retained all rights to and are developing on our own our current product candidates, we may in the future enter into development, distribution or marketing arrangements with third parties with respect to our other existing or future product candidates. Our likely collaborators for any such sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we enter into any such arrangements with any third parties in the future, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators’ abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Collaborations that we enter into, including our collaboration with MyoKardia, may not be successful, and any success will depend heavily on the efforts and activities of such collaborators. Collaborations pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development of our product candidates or may elect not to continue or renew development programs based on results of clinical trials or other studies, changes in the collaborators’ strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may not pursue commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew commercialization programs based on results of clinical trials or other studies, changes in the collaborators’ strategic focus or available funding, or external factors, such as an acquisition, that may divert resources or create competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates on a discretionary basis;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates and products if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over intellectual property or proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly obtain, maintain, enforce, defend or protect our intellectual property or proprietary rights or may use our proprietary information in such a way as to potentially lead to disputes or legal proceedings that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property or proprietary rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator (e.g., termination of our collaboration with Acceleron following its acquisition by Merck), and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. If any collaborations that we enter into do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed and we may need additional resources to develop our product candidates. All of the risks relating to product development, regulatory approval and commercialization described herein also apply to the activities of our collaborators.

Additionally, subject to its contractual obligations to us, if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. For example, in November 2020, subsequent to our entering into the MyoKardia collaboration agreement, MyoKardia was acquired by Bristol-Myers Squibb Company. Bristol-Myers Squibb Company could determine to reprioritize MyoKardia's development programs such that it ceases to diligently pursue the development of our programs and/or cause the agreement between MyoKardia and us to terminate. If our collaborator terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

If we are not able to establish or maintain collaborations, we may have to alter our development and commercialization plans and our business could be adversely affected.

For some of our product candidates, we may decide to collaborate with pharmaceutical or biotechnology companies for the development and potential commercialization of those product candidates. For example, in July 2020, we entered into a collaboration and license agreement with MyoKardia to identify and validate potential biological targets for the potential treatment of certain genetically defined cardiomyopathies. We face significant competition in seeking appropriate collaborators, and a number of more established companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we consider attractive. These established companies may have a competitive advantage over us due to their size, financial 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. 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, 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 collaborator 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.

We may also be restricted under existing or future license agreements from entering into agreements on certain terms with potential collaborators. For example, we are restricted by GSK's right of first negotiation under our current license agreement with them, and we had restrictions under our collaboration with Acceleron. Under our collaboration with MyoKardia, we are restricted from researching, developing, manufacturing, commercializing, using, or otherwise exploiting any compound or product (a) that is a compound or product under the agreement that is directed against certain targets identified by us in the performance of the research activities for the treatment, prophylaxis, or diagnosis of any indication or (b) for the treatment of any genetically defined cardiomyopathies shown to be related to certain specified genes of interest that are modulated by the targets chosen by MyoKardia under our collaboration, in each case , while we are performing the research activities pursuant to the research plan and for a specified period thereafter.

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

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms or at all, we may have to curtail the development of a product candidate, 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 fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market.

Risks Related to our Intellectual Property

If we are unable to obtain, maintain, enforce and protect patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.

Our success depends in large part on our ability to obtain and maintain protection of the intellectual property we may own solely and jointly with others or may license from others, particularly patents, in the United States and other countries with respect to any proprietary technology and product candidates we develop. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates that are important to our business and by in-licensing intellectual property related to our technologies and product candidates. If we are unable to obtain or maintain patent protection with respect to any proprietary technology or product candidate, our business, financial condition, results of operations and prospects could be materially harmed.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, defend or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce and defend the patents, covering technology that we license from third parties. Therefore, these in-licensed patents and applications may not be prepared, filed, prosecuted, maintained, defended and enforced in a manner consistent with the best interests of our business.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the scope of patent protection outside of the United States is uncertain and laws of foreign countries may not protect our rights to the same extent as the laws of the United States or vice versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than

United States law does. With respect to both owned and in-licensed patent rights, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. Further, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates. In addition, 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 published at all. Therefore, neither we nor our licensors can know with certainty whether either we or our licensors were the first to make the inventions claimed in the patents and patent applications we own or in-license now or in the future, or that either we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our owned and in-licensed patent rights are highly uncertain. Moreover, our owned and in-licensed pending and future patent applications may not result in patents being issued which protect our technology and product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. 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 and our ability to obtain, protect, maintain, defend and enforce our patent rights, narrow the scope of our patent protection and, more generally, could affect the value or narrow the scope of our patent rights. For information relating to our patent portfolio, see Item 1 “Business—Intellectual Property” in the 2022 Annual Report.

Moreover, we or our licensors may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. If the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. For example, while we believe that the specific and generic claims contained in our U.S. patent provide protection for the method of using losmapimod for the treatment of FSHD and while we also believe that the specific and generic claims contained in our issued and pending U.S. non-provisional and provisional applications provide protection for the pharmaceutical compositions and methods of use for pociredir, third parties may nevertheless challenge such claims. If any such claims are invalidated or rendered unenforceable for any reason, we will lose valuable intellectual property rights and our ability to prevent others from competing with us would be impaired.

Additionally, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if our owned and in-licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and in-licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our management and employees, even if the eventual outcome is favorable to us. 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 such candidates are commercialized. Furthermore, our competitors may be able to circumvent our owned or in-licensed patents by developing similar or alternative technologies or products in a non-infringing manner. As a result, our owned and in-licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing technology and products similar or identical to any of our technology and product candidates.

Patent terms may be inadequate to protect our competitive position on our 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. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. 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 such candidates are commercialized. 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. For example, the composition of matter patents covering losmapimod, licensed from GSK have expired and are no longer a barrier to entry for any new uses not covered by our other patents and patent applications.

If we are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could harm our business, financial condition, results of operations and prospects significantly.

Additionally, if we fail to comply with our obligations under license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements, or restrictions on our ability to freely assign or sublicense our rights under such agreements when it is in the interest of our business to do so, may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology or impede, or delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements.

Under our current license agreements, we may not have the final or sole decision on whether we are able to opt out certain of our in-licensed European patents and patent applications from the recently created Unified Patent Court, or the UPC, for the European Union. While our licensors have decided to opt out of the UPC, we cannot guarantee that our in-licensed European patents and patent applications will be challenged for non-compliance during the opt-out procedure and if successful, brought under the jurisdiction of the UPC, nor can we guarantee that our licensors will decide to opt back into the UPC at a later time. Thus, we cannot be certain that our in-licensed European patents and patent applications will not fall under the jurisdiction of the UPC. Under the UPC, a single European patent would be valid and enforceable in numerous European countries. A challenge to the validity of a European patent under the UPC, if successful, could result in a loss of patent protection in numerous European countries which could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, our business may be materially harmed.

In the United States, the patent term of a patent that covers an FDA-approved drug may be eligible for limited patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to, among other factors, the length of time the drug is under regulatory review, but such patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one eligible patent may be extended. Similar provisions are available in Europe and certain other jurisdictions outside the United States. If and when our product candidates receive FDA approval, we expect to apply for patent term extensions where applicable, but there is no guarantee that the applicable governmental authorities will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. We may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations and prospects could be materially harmed.

Further, for our licensed patents, we may not have the right to control prosecution, including filing with the USPTO a petition for patent term extension thus if one of our licensed patents is eligible for patent term extension, we may not be able to control whether a petition to obtain a patent term extension is filed, or obtained, from the USPTO.

There are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Orange Book. We may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If one of our product candidates is approved and a patent covering that product candidate is not listed in the Orange Book, an ANDA applicant would not have to provide notice to us with respect to that patent. See Item 1 “Business—Intellectual Property” in the 2022 Annual Report for additional information regarding patent laws and patent protection.

Our issued European patents could be subject to the jurisdiction of the UPC.

Our European patents and patent applications could be challenged in the UPC. We decided to remove, i.e., opt out, our European patents and patent applications from the jurisdiction of the UPC. However, if certain formalities and requirements are not met, our European patents and patent applications could be challenged for non-compliance and brought under the jurisdiction of the UPC. We cannot be certain that our European patents and patent applications will avoid falling under the jurisdiction of the UPC. Under the UPC, a granted European patent would be valid and enforceable in numerous European countries. Although such patent rights would apply to numerous European countries, a successful challenge to a European patent under the UPC could result in loss of patent protection in numerous European countries. Accordingly, a single proceeding under the UPC addressing the validity and infringement of the European patent could result in loss of patent protection in numerous European countries rather than in each validated country separately as such patents always have been adjudicated. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

Changes to patent laws in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of patent laws in the United States, including patent reform legislation such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, could increase the uncertainties and costs surrounding the prosecution of our owned and in-licensed patent applications and the maintenance, enforcement or defense of our owned and in-licensed issued patents. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

Although we or our licensors are not currently involved in any litigation to protect or enforce our patent or other intellectual property rights, we may become involved in such lawsuits, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our or our licensor's issued patents or other intellectual property. As a result, we or our licensors may need to file infringement, misappropriation or other intellectual property related claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke such parties to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their intellectual property. In addition, in a patent infringement proceeding, such parties could counterclaim that the patents we or our licensors have asserted are 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. Third parties may institute such claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (*e.g.*, opposition proceedings). The outcome following legal assertions of invalidity and unenforceability is unpredictable.

An adverse result in any such proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly, and could put any of our owned or in-licensed patent applications at risk of not yielding an issued patent. A court may also refuse to stop the third party from using the technology at issue in a proceeding on the grounds that our owned or in-licensed patents do not cover such technology. 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 or trade secrets could be compromised by disclosure during this type of litigation. Any of the foregoing could allow such third parties to develop and commercialize competing technologies and products and have a material adverse impact on our business, financial condition, results of operations and prospects.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference or derivation proceedings may fail and, even if successful, may result in substantial costs and 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 development partnerships that would help us bring our product candidates to market.

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. 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 our common stock.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, 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 and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. There is considerable patent and other intellectual property litigation in the pharmaceutical and biotechnology industries. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and product candidates, including interference proceedings, post grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the European Patent Office. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our technologies or product candidates that we may identify may be subject to claims of infringement of the patent rights of third parties.

The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. The risks of being involved in such litigation and proceedings may increase if and as our product candidates near commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of merit. We may not be aware of all such intellectual property rights potentially relating to our technology and product candidates and their uses, or we may incorrectly conclude that third party intellectual property is invalid or that our activities and product candidates do not infringe such intellectual property. Thus, we do not know with certainty that our technology and product candidates, or our development and commercialization thereof, do not and will not infringe, misappropriate or otherwise violate any third party's intellectual property.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations or methods, such as methods of manufacture or methods for treatment, related to the discovery, use or manufacture of the product candidates that we may identify or related to our technologies. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that the product candidates that we may identify may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, as noted above, there may be existing patents that we are not aware of or that we have incorrectly concluded are invalid or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover, for example, the manufacturing process of the product candidates that we may identify, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize the product candidates that we may identify. 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. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may choose to take a license or, if we are found to infringe, misappropriate or otherwise violate a third party's intellectual property rights, we could also be required to obtain a license from such third party to continue developing, manufacturing and marketing our technology and product candidates. However, we may not be able to obtain any required license 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 could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right and could be forced to indemnify our customers or collaborators. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. In addition, we may be forced to redesign our product candidates, seek new regulatory approvals and indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations and prospects.

Intellectual property litigation or other legal proceedings relating to intellectual property could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and may also have an advantage in such proceedings due to their more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of intellectual property litigation or other proceedings could compromise our ability to compete in the marketplace.

Obtaining and maintaining 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, renewal and annuity fees and various other government fees on any issued patent and pending patent application must be paid to the USPTO and foreign patent agencies in several stages or annually over the lifetime of our owned and in-licensed 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 process. In certain circumstances, we rely on our licensing partners to pay these fees to, or comply with the procedural and documentary rules of, the relevant patent agency. With respect to our patents, we rely on an annuity service, outside firms and outside counsel to remind us of the due dates and to make payment after we instruct them to do so. While an inadvertent lapse can in many 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. In such an event, potential competitors might be able to enter the market with similar or identical products or technology. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, it would have a material adverse effect on our business, financial condition, results of operations and prospects.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, or otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.

We are party to license and funding agreements, such as our agreement with GSK and our recent license agreement with CAMP4, and we may enter into additional licensing and funding arrangements with third parties that impose or may impose diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Under our existing licensing and funding agreements, we are obligated to pay royalties on net product sales of product candidates or related technologies to the extent they are covered by the agreements. If we fail to comply with such obligations under current or future license and funding agreements, our counterparties may have the right to terminate these agreements or require us to grant them certain rights. Such an occurrence could materially adversely affect the value of any product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, which would have a material adverse effect on our business, financial condition, results of operations and prospects. We also have licenses and agreements to certain technologies that we use in our discovery efforts, all of which are non-exclusive. While we still face all of the risks described herein with respect to those agreements, we cannot prevent third parties from also accessing those technologies. In addition, our licenses may place restrictions on our future business opportunities. For example, under our license with GSK, GSK has certain rights of first negotiation if we wish to sublicense any of the patent or data rights licensed by GSK to us to a third party for use outside the United States. This may prevent or delay certain transactions, which could have an adverse effect on the development and commercialization of losmapimod and on our business.

Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements 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 technology, or increase what we believe to be our financial or other obligations under the relevant 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 arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected technology and product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

Our current or future licensors may have relied on third-party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents and patent applications we in-license. If other third parties have ownership rights to patents or patent applications we in-license, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize product candidates and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products and technologies identical to ours. This could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

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

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, and even where such protection is nominally available, judicial and governmental enforcement of such intellectual property rights may be lacking. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our 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 have patent protection or licenses but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries and in Russia, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. In addition, certain jurisdictions do not protect to the same extent or at all inventions that constitute new methods of treatment.

Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. 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. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that our employees, consultants or contractors have wrongfully used or disclosed confidential information of third parties, or we have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors were previously employed at universities or other pharmaceutical or biotechnology companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees, consultants and contractors who may be involved in the 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 develops intellectual property that we regard as our own. Our intellectual property assignment agreements with them may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims 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 conditions, results of operations and prospects.

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, which could have a material adverse effect on our competitive business position and prospects. 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, which license may not be available on commercially reasonable terms, or at all, or such license may be non-exclusive. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and employees.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information, to maintain our competitive position, including certain aspects of our discovery technology. We seek to protect our trade secrets and other proprietary technology, 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, CROs, CMOs, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants, but we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Detecting the disclosure or misappropriation of a trade secret and 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 inside and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

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 product candidates that are similar to ours but that are not covered by the claims of the patents that we own;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent applications that we license or may own in the future;
- we, or our license partners or 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 in-licensed intellectual property rights;
- it is possible that our owned and in-licensed pending patent applications or those we may own or in-license 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 cannot ensure that any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our product candidates;
- we cannot ensure that any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable product candidates or will provide us with any competitive advantages;
- we cannot ensure that our commercial activities or product candidates will not infringe upon the patents of others;
- we cannot ensure that we will be able to successfully commercialize our product candidates on a substantial scale, if approved, before the relevant patents that we own or license expire;
- portions of our discovery technology are protected by trade secrets, but much is not protected by intellectual property, including patents, trade secrets and know-how, and we may not be able to develop, acquire or in-license any patentable technologies or other intellectual property related to the unprotected portions of our discovery portfolio;
- 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 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.

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

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain, and we may not obtain approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Marketing approval of drugs in the United States requires the submission of a new drug application, or NDA, to the FDA and we are not permitted to market any drug candidate in the United States until we obtain approval of the NDA. An NDA must be supported by extensive clinical and preclinical data, as well as extensive information regarding pharmacology, chemistry, manufacturing and controls. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction.

We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party clinical research organizations or other third-party consultants or vendors to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information, including manufacturing information, to regulatory authorities for each therapeutic indication to establish the product candidate’s safety and efficacy. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Disruptions at the FDA and other agencies may prolong the time necessary for regulatory submissions to be reviewed and/or new drugs to be approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown were to occur, 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.

During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to a future pandemic or an outbreak of highly infectious or contagious disease, and may experience delays in their regulatory activities.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

We may not be able to obtain or maintain orphan drug designation or exclusivity for our product candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Regulatory authorities in some jurisdictions, including the United States and European Union, may designate drugs for relatively small patient populations as orphan drugs. The FDA and EMA have granted orphan drug designation to losmapimod for the treatment of FSHD. We may seek orphan drug designation for our other current and future product candidates.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of market exclusivity, which precludes the FDA or the EMA from approving another marketing authorization application for the same drug for a certain time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years at the end of the fifth year if it is determined that a drug no longer meets the criteria for orphan drug designation, including if the drug is sufficiently profitable so that market exclusivity is no longer justified. Proposed amendments to European Union regulations regarding orphan medicines are under consideration that could reduce the ten-year marketing exclusivity period to eight to nine years (or even as little as three to five years for well-established medicines). The European Union's April 2023 draft legislative proposal is under review, including by the European Parliament and European Council but, if implemented in due course, may mean that orphan medicines have reduced marketing exclusivity.

Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because competing drugs containing a different active ingredient can be approved for the same condition. In addition, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior to the first drug to obtain orphan drug exclusivity because it is shown to be safer, more effective or makes a major contribution to patient care. Moreover, if we pursue and obtain approval for the same product for another indication for which we are not entitled to or do not have orphan drug exclusivity, our period of orphan exclusivity will not prevent third parties from obtaining approval for a competing drug containing the same active ingredient for use in this other, non-orphan indication. If that were to occur, the protection we derive from orphan exclusivity may be adversely affected.

Special designation by the FDA, such as fast track or breakthrough therapy, may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

The FDA granted fast track designation to losmapimod for the treatment of FSHD and to pociredir for the treatment of SCD, and we may seek fast track designation for some of our other product candidates as well as breakthrough therapy designation, including for losmapimod. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA 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, we cannot assure stockholders that the FDA would decide to grant it. Even with fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

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. Even if we receive breakthrough therapy designation, the receipt of such designation for a product candidate may not result in a faster development process, review or approval compared to drugs 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 the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Even if the FDA agrees that we may pursue an accelerated approval NDA submission, approval of the NDA is not assured, nor does submission of an accelerated approval NDA ensure that the product candidate will have a faster development or regulatory review process.

We may seek approval, as applicable, of our product candidates using the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious 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 or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit (*i.e.*, an intermediate clinical endpoint).

Prior to seeking such accelerated approval, we will seek feedback from the FDA and otherwise evaluate our ability to seek and receive such accelerated approval.

There can be no assurance that, after feedback from FDA, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation, there can be no assurance that such submission or application will be accepted or that any expedited review or approval will be granted on a timely basis, or at all.

Moreover, as a condition of accelerated approval, the FDA likely would require that we perform adequate and well-controlled post-marketing clinical trials to confirm the product's clinical benefit. 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. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted 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. Under FDORA, 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. In addition, the FDA generally requires pre-approval of promotional materials for products under consideration for 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 for a product candidate, we may not experience a faster development or regulatory review or approval process for that product. In addition, receiving accelerated approval does not assure that the product's accelerated approval will ultimately be converted to a traditional approval.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad.

In order to market and sell our products in the European Union and many other foreign jurisdictions, we or our potential third-party collaborators 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 of the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside of the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or our potential third-party collaborators may not obtain approvals, including conditional authorization, from regulatory authorities outside of the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in other countries. We may not be able to file for marketing approvals and may not receive the necessary approvals to commercialize our products in any market.

Additionally, now that the United Kingdom is no longer part of the European Union, separate applications and procedures will be required to obtain regulatory approval for our products in the United Kingdom and the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals could prevent us from commercializing any product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product, including the adoption and implementation of REMS. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. Violations of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may have various consequences, including:

- suspension of or restrictions on such products, manufacturers or manufacturing processes;
- restrictions and warnings on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension of any ongoing clinical trials;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;

- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure or detention;
- injunctions or the imposition of civil or criminal penalties; or
- litigation involving patients using our products.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's or United Kingdom's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs applicable to drug manufacturers. Additionally, under FDORA, sponsors of approved drugs and biologics must provide six months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product's ability to be marketed. We will also be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to clinicians, and recordkeeping.

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

If we obtain regulatory approval and commercialize any products, 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 future arrangements with healthcare providers, physicians and third-party payors 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 market, sell and distribute any products for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by U.S. federal and state governments and by governments in foreign jurisdictions in which we conduct our business. See Item 1 "Business—Government Regulation and Product Approvals—Health Care Law and Regulation" in the 2022 Annual Report.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Efforts to ensure that our business arrangements with third parties will 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 involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities that would be conducted by our sales team, are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government funded healthcare programs.

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

The legislative and regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Economic Area, or EEA, including personal health data, is subject to the European Union's General Data Protection Regulation, or EU GDPR. Following the withdrawal of the United Kingdom from the European Union, or Brexit, the EU GDPR has been incorporated into

United Kingdom's laws, or UK GDPR, alongside the UK Data Protection Act 2018, and together with the EU GDPR, is referred to as GDPR.

Despite Brexit, the EU and UK GDPR remain largely aligned. Currently, the most impactful point of divergence relates to transfer mechanisms (i.e., the ability for companies in the European Union or the United Kingdom to transfer personal information to third countries, including the United States), because it requires us to implement a variety of different contractual clauses approved by European Union's or United Kingdom's regulators, and carry out transfer impact assessments to establish whether the third country can ensure essential equivalency. This complexity and the additional contractual burden increases our overall risk exposure, and may result in us needing to make strategic considerations around where EEA and UK personal data is stored and which service providers we can utilize for the processing of EEA and UK personal data.

There may be further divergence in the future, including with regard to administrative burdens. The UK Government has also now introduced a Data Protection and Digital Information Bill, or the 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. This may lead to additional compliance costs and could increase our overall risk exposure as we may no longer be able to take a unified approach across the European Union and the United Kingdom, and we will need to amend our processes and procedures to align with the new framework.

Similar data protection laws are either in place or under way in the United States. There are a broad variety of privacy and data security laws and regulations that may be applicable to our activities governing the collection, use, disclosure, and protection of health-related and other personal information (including, state data breach notification laws, health information and/or genetic privacy laws and federal and state consumer protection laws including Section 5 of the FTC Act, HIPAA, and the California Consumer Privacy Act, or CCPA). For example, the CCPA as amended by the California Privacy Rights Act, has created certain requirements for data use, sharing and transparency, and provides California residents certain rights concerning their personal information. Many other states, including Virginia, Colorado and Connecticut, have implemented privacy legislation similar to the CCPA, and various other U.S. states are either preparing to implement their own regulatory frameworks or are considering similar legislation. A wide range of enforcement agencies at both the state and federal levels can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. For more information regarding the GDPR, the CCPA and other regulations, see Item 1 "Business –Government Regulation and Product Approvals" in the 2022 Annual Report.

Given the breadth and depth of changes in privacy, data protection and consumer protection obligations, preparing for and complying with these requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that store, process or transfer personal data on our behalf. Many of these laws differ from each other in significant ways and may be interpreted and applied in a manner that is inconsistent from one jurisdiction to another, thus complicating compliance efforts. Compliance with the GDPR and other similar laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business. Any failure or perceived failure by us to comply with such laws and regulations could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations. There is also the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

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

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any FDA approved product. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed. See Item 1 "Business—Government Regulation and Product Approval—Pharmaceutical Insurance Coverage and Health Care Reform" in the 2022 Annual Report.

In August 2022 the Inflation Reduction Act of 2022 was passed, which among other things, allows for Centers for Medicare & Medicaid Services to negotiate prices for certain single-source drugs and biologics reimbursed under Medicare Part B and Part D, beginning with select high-cost drugs in 2026. The legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for offering a price that is not equal to or less than the price negotiated under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. Further, the legislation caps Medicare beneficiaries' annual out-of-pocket drug expenses at $2,000. 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 Inflation Reduction Act of 2022 on our business and the healthcare industry in general is not yet known.

In addition, multiple executive orders have been issued that seek to reduce prescription drug costs. In February 2023, HHS also issued a proposal in response to an October 2022 executive order 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 current administration may reverse or otherwise change these measures, both the current administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

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

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

In countries outside of the United States, particularly the countries of the European Union, 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 product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

If we or any third-party manufacturers we engage now or in the future fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs or liabilities that could harm our business.

We and third-party manufacturers we engage now are, and any third-party manufacturers we may engage in the future will be, subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Liability under certain environmental laws governing the release and cleanup of hazardous materials is joint and several and could be imposed without regard to fault. We also could incur significant costs associated with civil or criminal fines and penalties or become subject to injunctions limiting or prohibiting our activities for failure to comply with such laws and regulations.

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

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

Further, with respect to the operations of our current and any future third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of our product candidates or products. In addition, our supply chain may be adversely impacted if any of our third-party contract manufacturers become subject to injunctions or other sanctions as a result of their non-compliance with environmental, health and safety laws and regulations.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, be precluded from developing manufacturing and selling certain products outside the United States or be required to develop and implement costly compliance programs, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act, the U.S. Foreign Corrupt Practices Act, or FCPA, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Bribery Act, FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. Compliance with the FCPA, in particular, is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

We may in the future operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted. If we expand our operations outside of the United States, we will need to dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws. In addition, various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by United Kingdom, United States or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

Our employees, independent contractors, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants and vendors. Misconduct by these partners could include intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the EU GDPR. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us. 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 governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards, regulations, guidance or codes of conduct. 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 and results of operations, including the imposition of significant fines or other sanctions.

Our internal computer and information technology systems and infrastructure, or those of our collaborators or other contractors or consultants, may fail or suffer security compromises or breaches, which could result in a material disruption of our product development programs.

Our internal computer and information technology systems and infrastructure and those of our CROs, collaborators, and other contractors or consultants upon which our business relies, are vulnerable to breakdown or damage or interruption or otherwise may sustain damage from computer viruses, unauthorized access, data breaches, phishing attacks, cybercriminals, system malfunction, natural disasters (including hurricanes and earthquakes), terrorism, war and telecommunication and electrical failures. Such systems and infrastructure are also vulnerable to service interruptions or to security compromises or breaches from inadvertent or intentional actions by our employees, CROs or other third-party vendors, contractors, consultants and/or business partners or other third parties, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include wrongful conduct by insider employees or vendors, hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud or cyber-attacks, including the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, phishing attacks and social engineering, business email compromise, and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Accordingly, if our cybersecurity measures or those of our service providers fail to protect against unauthorized access, attacks, compromise or the mishandling of data by our employees or contractors, then our reputation, customer trust, business, results of operations and financial condition could be adversely affected. Because the techniques used by threat actors who may attempt to penetrate and sabotage our computer systems or those of our collaborators or other contractors or consultants change frequently and may not be recognized until launched against a target, we may be unable to anticipate these techniques. For example, we make extensive use of cloud-based storage systems, and in October 2018, we experienced a breach of one such system. While this breach did not result in the permanent loss or theft of any of our critical information or any other material consequences, it could have, and while we took steps to remediate this breach, such as establishing multi-factor authentication and implementing improvements to our data securities protocols, we cannot guarantee that the measures we have taken to date, and actions we may take in the future, will be sufficient to remediate any future breaches.

While we have not experienced any material system failure, accident, cyber-attack 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, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security compromise or breach were to result in a loss of, damage to, unauthorized access, or misuse of our data, systems, infrastructure or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability (including in connection with or resulting from litigation or governmental investigations and enforcement actions), our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed and our business could be otherwise adversely affected.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical, financial, operational and other business expertise of our executive officers, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment offer letters with our executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel will also be critical to our success.

We have had recent executive transitions, including of our chief executive officer, chief financial officer, president of research and development, chief scientific officer, and chief medical officer. We cannot predict the likelihood, timing or effect of future transitions among our executive leadership. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. For example, our employees have taken on increased responsibilities in light of this turnover, which could divert attention from key business areas. Additionally, the number of recent departures has created some uncertainty. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Even if we are successful in our efforts to replace our executive leadership, we cannot guarantee that we will not face similar turnover in the future. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. In August 2022, we announced a workforce reduction in our research and development function, which may make us a less attractive employer to future candidates. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Our success as a public company also depends on implementing and maintaining internal controls and the accuracy and timeliness of our financial reporting. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to our Common Stock

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control or significantly influence all matters submitted to stockholders for approval.

As of October 31, 2023, our executive officers and directors and our stockholders who owned more than 5% of our outstanding common stock in the aggregate beneficially owned shares representing approximately 54.6% of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and board of directors; or
- delay or prevent a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current directors and members of management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or the DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

If securities analysts do not publish or cease publishing research or reports or publish misleading, inaccurate or unfavorable research about our business or if they publish negative evaluations of our stock, the price and trading volume of our stock could decline.

The trading market for our common stock relies, in part, on the research and reports that industry or financial analysts publish about us or our business. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analyst will provide favorable coverage. Although we have obtained analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock or publish inaccurate or unfavorable research about our business, or provides more favorable relative recommendations about our competitors, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price and trading volume to decline.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.

The trading price of our common stock has been, and is likely to continue to be volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- results of or developments in preclinical studies and clinical trials of our product candidates or those of our competitors or potential collaborators;
- our success in commercializing our product candidates, if and when approved;
- the success of competitive products or technologies;

- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license products, product candidates, technologies or data referencing rights, the costs of commercializing any such products and the costs of development of any such product candidates or technologies;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation has often been instituted against that company. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our offerings or business practices. Such litigation may also cause us to incur other substantial costs to defend such claims and divert management's attention and resources. Furthermore, negative public announcements of the results of hearings, motions or other interim proceedings or developments could have a negative effect on the market price of our common stock.

A significant portion of our total outstanding shares are eligible to be sold into the market, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Persons who were our stockholders prior to our initial public offering continue to hold a substantial number of shares of our common stock. If such persons sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline.

In addition, we have filed or intend to file universal shelf registration statements (which allows us to offer and sell securities from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale) subject to an aggregate offering amount stated therein, as well as registration statements registering all shares of common stock that we may issue under our equity compensation plans or pursuant to equity awards made to newly hired employees outside of equity compensation plans. Such registered shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an EGC until December 31, 2024, although if the market value of our common stock that is held by non-affiliates exceeds $700 million as of any June 30 before that time or if we have annual gross revenues of $1.235 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than $1 billion of non-convertible debt over a three-year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply 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;

- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may choose to take advantage of some or all of the available exemptions. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected not to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an EGC.

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

As a public company we have incurred, and particularly after we are no longer an EGC, we will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements, and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an EGC or a smaller reporting company with less than $100 million in revenue, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we conduct a process each year to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, including through hiring additional financial and accounting personnel, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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

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

Our certificate of incorporation designates the state courts in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors, officers and employees.

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware or (4) any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. This exclusive forum provision will not apply to actions arising under the Securities Act or the Securities Exchange Act of 1934, as amended.

This exclusive forum provision may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find the choice of forum provision contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition and operating results.

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

Not applicable.

Item 3. Defaults Upon Senior Securities.

Not applicable.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

None.

Item 6. Exhibits.

Exhibit Number	Description
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 22, 2019).
3.2	Certificate of Amendment of the Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 9, 2023).
3.3	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 22, 2019).
10.1*†	License Agreement, effective as of July 5, 2023, by and between the Registrant and CAMP4 Therapeutics Corporation.
10.2*#	Employment Agreement, dated August 7, 2023, by and between the Registrant and Alan A. Musso.
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 Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
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 Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1+	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2+	Certification of 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.
# Management contract or compensatory plan or arrangement.
† Certain portions of this exhibit have been omitted because the registrant has determined that they are both not material and is the type of information that the registrant treats as private or confidential.
+ Furnished herewith.

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.

FULCRUM THERAPEUTICS, INC.

Date: November 7, 2023	By:	/s/ Alex C. Sapir
		Alex C. Sapir
		President and Chief Executive Officer (Principal Executive Officer)
Date: November 7, 2023	By:	/s/ Alan Musso
		Alan Musso
		Chief Financial Officer (Principal Financial Officer)

Exhibit 10.1

CERTAIN INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) IS THE TYPE THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL

LICENSE AGREEMENT

between

CAMP4 THERAPEUTICS CORP.

and

FULCRUM THERAPEUTICS INC.

LICENSE AGREEMENT

This **License Agreement** ("***Agreement***") is entered into as of July 5th, 2023 (the "***Effective Date***") by and between **CAMP4 Therapeutics Corporation**, a corporation organized and existing under the laws of Delaware, with its principal business office located at One Kendall Square, Bldg 1400 West, 3rd Floor, Cambridge, MA 02139, U.S.A. ("***CAMP4***"), and **Fulcrum Therapeutics, Inc.**, a corporation organized and existing under the laws of Massachusetts, with its principal business office located at 26 Landsdowne Street Cambridge, MA 02139, U.S.A. ("***Fulcrum***"). Fulcrum and CAMP4 are each hereafter referred to individually as a "***Party***" and together as the "***Parties***."

Whereas, CAMP4 is a biotechnology company engaged in the research and development of therapeutics for treatment of various diseases;

Whereas, Fulcrum is a clinical-stage biopharmaceutical company engaged in the research, development, manufacturing, marketing and distribution of precision medicines in areas of high unmet medical need;

Whereas, CAMP4 wishes to license to Fulcrum rights under its Diamond Blackfan Anemia (DBA) program, which includes certain small molecule compounds, composition of matter and method of use patent rights, and know-how for Fulcrum to develop and commercialize therapeutic products in any indication, including the grant of a sublicense under certain intellectual property rights that CAMP4 has licensed under the CMCC License Agreement (as defined below); and

Whereas, Fulcrum desires to obtain from CAMP4, and CAMP4 desires to grant to Fulcrum, an exclusive license to certain intellectual property rights and know-how to research, develop, manufacture, and commercialize Licensed Products (as defined below), subject to the terms and conditions of this Agreement.

Now, Therefore, in consideration of the mutual covenants contained herein, and for other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, the Parties hereby agree as follows:

ARTICLE 1

DEFINITIONS

Capitalized terms used in this Agreement and the Exhibits hereto shall have the following meanings (or as defined elsewhere in this Agreement):

1.1 "***Acquired Party***" has the meaning set forth in Section 2.6.2.

1.2"***Affiliate***" means, with respect to either Party, any entity that, at the relevant time (whether as of the Effective Date or thereafter), directly or indirectly through one or more intermediaries, controls, is controlled by, or is under common control with such Party, for so long as such control exists. As used in this Section 1.2, "control" means: (a) to possess, directly or indirectly, the power to direct or cause the direction of the management or policies of an entity, whether through ownership of voting securities or by contract relating to voting rights or corporate governance; or (b) direct or indirect ownership of fifty percent (50%) (or such lesser percentage that is the maximum allowed to be owned by a foreign entity in a particular jurisdiction) or more of the voting share capital or other equity interest in such entity.

1.3 "***Agreement***" has the meaning set forth in the Preamble.

1.4"***Applicable Laws***" means the applicable provisions of any and all federal, national, supranational, regional, state, provincial and local laws, treaties, statutes, rules, regulations, guidelines or requirements, administrative codes, guidance, ordinances, judgments, decrees, directives, injunctions, orders, or permits of or from any court, arbitrator, Regulatory Authority, Governmental Authority, taxing authority, securities exchange or exchange listing organization having jurisdiction over or related to the relevant subject item that may be in effect from time to time during the Term.

1.5"***Business Day***" means any day other than Saturday, Sunday, or any day that banks are authorized or required to be closed in Cambridge, Massachusetts, U.S.A.

1.6"***Calendar Quarter***" means each respective period of three (3) consecutive months ending on March 31, June 30, September 30, and December 31 of any Calendar Year.

1.7"***Calendar Year***" means each respective period of twelve (12) consecutive months commencing on January 1 and ending on December 31.

1.8 "***CAMP4***" has the meaning set forth in the Preamble.

1.9 "***CAMP4 Indemnitee***" has the meaning set forth in Section 7.1.6.

1.10"***CAMP4-Assignee Patents"*** means (i) the Patents listed in Part A of Exhibit A; and (ii) any other Patents, other than any CMCC-Licensed Patents, Controlled by CAMP4 or its Affiliates as of the Effective Date or that become Controlled by CAMP4 or its Affiliates at any time during the Term that are necessary or reasonably useful for the Development, Manufacture or Commercialization of a Licensed Product.

1.11"***CAMP4 Know-How***" means any other Know-How Controlled by CAMP4 or its Affiliates as of the Effective Date or that becomes Controlled by CAMP4 or its Affiliates at any time during the Term that is necessary or reasonably useful for the Development, Manufacture or Commercialization of a Licensed Product developed pursuant to this Agreement, including for clarity the information listed in Exhibit B.

1.12"***Change of Control***" means: (a) with respect to a Party, the acquisition by a Third Party, in one transaction or a series of related transactions, of direct or indirect beneficial ownership of more than fifty percent (50%) of the outstanding securities or combined voting power of such Party (or any controlling Affiliate of such Party); (b) a merger or consolidation or other business combination involving such Party, as a result of which a Third Party acquires direct or indirect beneficial ownership of more than fifty percent (50%) of the outstanding securities or combined voting power of the surviving entity immediately after such merger, reorganization or combination; or (c) a sale of all or substantially all of the assets of such Party related to this Agreement in one transaction or a series of related transactions to a Third Party. The acquiring or combining Third Party in any of (a), (b) or (c), and any of such Third Party's Affiliates (whether in existence as of or any time following the applicable transaction, but other than the acquired Party and its Affiliates as in existence prior to the applicable transaction or Affiliates it controls after the applicable transaction) are referred to collectively herein as the "***Acquirer***." As used in this definition, "control" means (1) to possess, directly or indirectly, the power to direct or cause the direction of the management or policies of an entity, whether through ownership of outstanding securities or voting power or by contract relating to voting rights or corporate governance; or (2) direct or indirect ownership of more than fifty percent (50%) of the outstanding securities or voting power interest in such entity.

1.13 "***Claims***" has the meaning set forth in Section 7.1.4.

1.14"***Clinical Trial***" means a Phase I Clinical Trial, Phase II Clinical Trial or Phase III Clinical Trial, or any post-Regulatory Approval human clinical trial, as applicable.

1.15"***CMCC***" means the Children's Medical Center Corporation, a charitable corporation having its principal office at 300 Longwood Avenue, Boston.

1.16 "***CMCC Indemnitee***" has the meaning set forth in Section 7.1.1.

1.17"***CMCC Know-How***" means all Know-How licensed to CAMP4 as of the Effective Date or at any time during the Term under the CMCC License Agreement.

1.18 "***CMCC-Licensed Patents***" means (i) the Patents listed in Part B of Exhibit A; and (ii) any other Patents that are licensed to CAMP4 as of the Effective Date or at any time during the Term pursuant to the CMCC License Agreement.

1.19"***CMCC License Agreement***" means the license agreement between CMCC and CAMP4, dated April 19, 2018 (the "***CMCC Agreement Effective Date***").

1.20 "***Commercial Milestone Event***" has the meaning set forth in Section 4.2.

1.21 "***Commercial Milestone Payment***" has the meaning set forth in Section 4.2.

1.22"***Commercialization***" means any and all activities directed to the offering for sale and sale of a Licensed Product, or other compound, product or therapy including: (a) activities directed to storing, marketing, promoting, detailing, distributing, importing, exporting, selling and offering to sell that Licensed Product, or other compound, product or therapy; (b) conducting Clinical Trials after Marketing Authorization of a Licensed Product, or other compound, product or therapy with respect to such Licensed Product, or other compound, product or therapy; (c) interacting with Regulatory Authorities regarding the foregoing; and (d) seeking Regulatory Approvals (as applicable) for and registration of that Licensed Product, or other compound, product or therapy beyond Marketing Authorization. For clarity, "Commercialization" does not include Development or Manufacturing activities. When used as a verb, "to ***Commercialize***" and "***Commercializing***" means to engage in Commercialization and "***Commercialized***" has a corresponding meaning.

1.23"***Commercially Reasonable Efforts***" of a Party means [***]. For clarity, "Commercially Reasonable Efforts" shall be [***].

1.24 "***Competing Product***" has the meaning set forth in Section 2.6.1.

1.25"***Confidential Information***" means all information (including chemical or biological materials, chemical structures correspondence, customer lists, data, formulae, improvements, inventions, Know-How, processes, Regulatory Approvals, Regulatory Filings, reports, strategies, techniques, or other information) that is disclosed by or on behalf of such Party or any of its Affiliates to the other Party or any of its Affiliates pursuant to this Agreement or the Mutual Confidentiality Agreement, regardless of whether any of the foregoing are marked "confidential" or "proprietary" or communicated to the other Party by or on behalf of the Disclosing Party in oral, written, visual, graphic or electronic form. Without limiting the generality of the foregoing, Confidential Information includes: (a) information acquired by Fulcrum from CMCC in the course of Prosecution and Maintenance of the CMCC-Licensed Patents; and (b) information disclosed to CAMP4 pursuant to Sections 2.2, 3.3, 4.5, 4.7, 7.2 or other reporting obligations under this Agreement.

1.26"***Control***" or "***Controlled***" means, with respect to any Know-How, Patents, or other intellectual property rights, that a Party has the legal authority or right (whether by ownership, license, or otherwise) to grant to the other Party a license, covenant not to sue, sublicense, access, or right to use (as applicable) under such Know-How, Patents, or other intellectual property rights, on the terms and conditions set forth herein without requiring any payment right to a Third Party arising from such Party's use or exploitation of such Know-How, Patent, or other intellectual property (other than all Know-How, Patent and other intellectual property rights licensed to CAMP4 pursuant to the CMCC License Agreement, which shall be deemed Controlled by CAMP4 as of the Effective Date), *provided* that, a Party or any of its Affiliates shall be deemed not to "Control" any Patent, Know-How, or other intellectual property right if such Patent, Know-How, or other intellectual property right is owned or in-licensed by an Acquirer of a Party that becomes an Affiliate of such Party (or that merges or consolidates with such Party) on or after the Effective Date as a result of a Change of Control of such Party, except to the extent, and only to the extent that, such Patent, Know-How, or other intellectual property right is (a) actually used by such Party or its Affiliates, or the Acquirer, to Develop, Manufacture, Commercialize, or otherwise exploit the Licensed Products following the consummation of such Change of Control or (b) made, conceived, or reduced to practice by the Acquirer or its Affiliates through the use of, or reference to, any Patent, Know-How, or other intellectual property right or Confidential Information of the other Party or (c) was Controlled by such Party or its Affiliates prior to the applicable Change of Control.

1.27"***Cover***" means, with respect to a given product, service or process, that a Valid Claim would, absent a license thereunder, be infringed by the manufacture, use, sale, offer for sale, importation or practice of such product, service or process.

1.28“***DBA Program***” means the research and development program conducted by CAMP4 under the CMCC-Licensed Patents and the CAMP4-Assignee Patents, focused on using [***] to rescue Diamond Blackfan Anemia disease states.

1.29“***Development***” or “***Develop***” means any and all activities directed to the non- clinical and clinical drug development activities that are necessary or useful to obtain Marketing Authorization for a Licensed Product, or other compound, product or therapy, including design and conduct of Clinical Trials and the preparation and filing of Regulatory Filings and all regulatory affairs related to the foregoing. For clarity, “Development” does not include Commercialization or Manufacturing activities. When used as a verb, ***“Developing”*** means to engage in Development and ***“Developed”*** has a corresponding meaning. For clarity, “***Development***” shall not include any Commercialization activities.

1.30 “***Development Milestone Event***” has the meaning set forth in Section 4.2.1.

1.31 “***Development Milestone Payment***” has the meaning set forth in Section 4.2.1.

1.32 “***Development Plan***” has the meaning set forth in Section 3.3.

1.33 “***Development Report***” has the meaning set forth in Section 3.3.

1.34“***DFCI***” means the Dana Farber Cancer Institute, a charitable corporation having its principal office at 450 Brookline Avenue, Boston.

1.35 “***Disclosing Party***” has the meaning set forth in Section 8.1.1.

1.36 “***Dispute***” has the meaning set forth in Section 10.2.

1.37 “***Dollar***” means a U.S. dollar, and “***$***” is to be interpreted accordingly.

1.38 “***Effective Date***” has the meaning set forth in the preamble to this Agreement.

1.39“***EMA Approval***” means the grant of Marketing Authorization by the European Medicines Agency.

1.40“***Executive Officers***” means the President and Chief Executive Officer of each Party (or in the event that these roles become held by separate people, either the President or the Chief Executive Officer for such Party).

1.41"***FDA***" means the United States Food and Drug Administration or any successor agency thereto.

1.42"***Field***" means all uses and purposes, including any and all uses for the diagnosis, prevention, amelioration, or treatment of any disease or medical condition in humans and animals.

1.43 "***First Commercial Sale***" means, with respect to a Licensed Product in any country: (i) the first sale of such Licensed Product by Fulcrum, its Affiliate, Sublicensee or authorized agent in that country, following Marketing Authorization of such Licensed Product if any such Marketing Authorization is necessary, for such country in which the sale is to be made; or (ii) when Marketing Authorization is not required, the first sale in that country of such Licensed Product by Fulcrum, its Affiliate, Sublicensee or authorized agent in that country, *provided* that the sale, disposal or use of any Licensed Product for marketing, regulatory, development or charitable purposes, such as clinical trials, preclinical trials, compassionate use, named patient use, expanded access programs or indigent patient programs, in each case at or below cost, shall not be deemed a First Commercial Sale.

1.44 "***Fulcrum***" has the meaning set forth in the Preamble.

1.45 "***Fulcrum Indemnitee***" has the meaning set forth in Section 7.1.5.

1.46"***Generic Product***" means, with respect to a Licensed Product, and on a Licensed Product-by-Licensed Product and country-by-country basis, any product (including a "generic product," "biogeneric," "follow-on biologic," "follow-on biological product," "follow-on protein product," "similar biological medicinal product," or "biosimilar product") approved by way of an abbreviated regulatory mechanism by the relevant Regulatory Authority in a country in reference to such Licensed Product, that in each case: (a) is sold in the same country (or is commercially available in the same country via import from another country) as such Licensed Product by any Third Party that is not a Sublicensee of Fulcrum or its Affiliates and that did not purchase such product in a chain of distribution that included any of Fulcrum or any of its Affiliates or its Sublicensees; and (b) either (i) contains an active ingredient that is highly similar to and has no clinically meaningful differences from the Licensed Product or (ii) meets the equivalency determination by the applicable Regulatory Authority in such country (including a determination that the product is "comparable," "interchangeable," "bioequivalent," "biosimilar" or other term of similar meaning, with respect to the Licensed Product), in each case, as is necessary to permit substitution of such product for the Licensed Product under Applicable Law in such country.

1.47[***]

1.48"***Governmental Authority***" means any federal, national, international, regional, state, provincial or local government, or political subdivision thereof, or any multinational organization or any authority, agency or commission entitled to exercise any administrative, executive, judicial, legislative, police, regulatory or taxing authority or power, and any court or tribunal (or any department, bureau or division thereof, or any governmental arbitrator or arbitral body).

1.49 “***Harvard***” means the President and Fellows of Harvard College.

1.50“***HHMI***” means the Howard Hughes Medical Institute, a private non-profit medical research organization having its principal office at 4000 Jones Bridge Rd, Chevy Chase, Maryland.

1.51 “***Indemnitee***” has the meaning set forth in Section 7.1.7.

1.52 “***Indemnitor***” has the meaning set forth in Section 7.1.7.

1.53 “***Infringement***” has the meaning set forth in Section 5.2.1.

1.54“***Know-How***” means any proprietary scientific or technical information, inventions, discoveries, results and data of any type whatsoever, in any tangible or intangible form, including inventions, discoveries, databases, safety information, practices, methods, instructions, techniques, processes, drawings, documentation, specifications, formulations, formulae, knowledge, know- how, trade secrets, materials, skill, experience, test data and other information and technology applicable to formulations, compositions or products or to their Research, Development, Manufacture, use, or Commercialization or to methods of assaying or testing them, including pharmacological, pharmaceutical, medicinal chemistry, biological, chemical, biochemical, toxicological and clinical test data, physical and analytical, safety, quality control data, manufacturing, and stability data, materials, studies and procedures, and manufacturing process and development information, results and data.

1.55 “***Japan Approval***” means the grant of Marketing Authorization in Japan.

1.56“***Licensed Patents***” means the CAMP4-Assignee Patents and the CMCC-Licensed Patents.

1.57 “***Licensed Product***” means any Tier 1 Product or Tier 2 Product.

1.58 “***Losses***” has the meaning set forth in Section 7.1.1.

1.59“***Major Market***” means each of the United States, Japan, United Kingdom, Germany, France, Italy and Spain.

1.60“***Manufacture***” and “***Manufacturing***” means all activities related to the production, manufacture, formulation, finishing, packaging, labeling, shipping and holding of any Licensed Product, or other compound, product or therapy, or any component, intermediary or precursor thereof, and including process development, process qualification and validation, scale- up, pre-clinical, clinical and commercial manufacture, quality assurance and quality control (including testing). For clarity, “Manufacturing” does not include Development or Commercialization activities.

1.61“***Marketing Authorization***” means any and all approvals, licenses, registrations or authorizations of any regulatory authority, necessary to commercially distribute, sell or market a Licensed Product in the relevant country or jurisdiction.

1.62“***Milestone Events***” means the Development Milestone Events and Commercial Milestone Events.

1.63“***Milestone Payments***” means the Development Milestone Payments, Commercial Milestone Payments and Sales Milestone Payments.

1.64“***Mutual Confidentiality Agreement***” means the Mutual Confidentiality Agreement dated [***] between Fulcrum and CAMP4.

1.65“***Net Sales***” means, as determined under U.S. generally accepted accounting principles (“GAAP”), the gross sales invoiced for sales, or other transfers of Licensed Products by Fulcrum, its Affiliates, its authorized agents, or its Sublicensees (for clarity, excluding sales by Third Party Distributors), less (to the extent actually allowed or incurred and directly related to such sale of Licensed Products) the following amounts: [***]

Net Sales shall also include [***] shall not be considered a Net Sale for purposes of ascertaining royalty charges owed to CAMP4 under this Agreement. For clarity, any payments received by Fulcrum, its Affiliates, or Sublicensees from [***]. Notwithstanding anything to the contrary herein, the sale, disposal or use of any Licensed Product for marketing, regulatory, development or charitable purposes, such as clinical trials, preclinical trials, compassionate use, named patient use, expanded access programs or indigent patient programs, in each case at or below cost, shall not be deemed a sale resulting in Net Sales hereunder.

In the event that the Licensed Product is sold as part of a Combination Product (where “***Combination Product***” means any pharmaceutical product which comprises the Licensed Product and other active compound(s)), the Net Sales of the Licensed Product, for the purposes of determining Royalty payments, shall be determined by multiplying the Net Sales of the Combination Product (as defined in the standard Net Sales definition) by [***].

In the event that [***] Net Sales for purposes of determining Royalty payments shall be calculated by [***].

In the event that [***] Net Sales for purposes of determining Royalty payments shall be calculated by [***].

If the [***], the Net Sales of the Licensed Product shall be [***].

[***] shall be calculated [***] and such [***] shall be used during all applicable Royalty reporting periods for [***]. When determining [***] of a Licensed Product, other compound(s), or Combination Product, [***] shall be calculated by [***].

1.66 “***New License Agreement***” has the meaning set forth in Section 9.8.1.

1.67“***Party***” and “***Parties***” has the meaning set forth in the Preamble.

1.68“***Patents***” mean: (a) pending patent applications, issued patents, utility models and designs; (b) reissues, substitutions, confirmations, registrations, validations, re-examinations, additions, continuations, continued prosecution applications, continuations-in-part, or divisions of or to any of the foregoing; and (c) extensions, renewals or restorations of any of the foregoing by existing or future extension, renewal or restoration mechanisms, including supplementary protection certificates or the equivalent thereof.

1.69“***Person***” means any corporation, limited or general partnership, limited liability company, joint venture, trust, unincorporated association, governmental body, authority, bureau or agency, any other entity or body, or an individual.

1.70“***Phase I Clinical Trial***” means a clinical trial of a Licensed Product generally consistent with 21 C.F.R. § 312.21(a) (or the non-United States equivalent thereof).

1.71“***Phase II Clinical Trial***” means a clinical trial of a Licensed Product generally consistent with 21 C.F.R. § 312.21(b) (or the non-United States equivalent thereof).

1.72“***Phase III Clinical Trial***” means a clinical trial of a Licensed Product generally consistent with 21 C.F.R. § 312.21(c) (or the non-United States equivalent thereof).

1.73“***Pricing and Reimbursement Approval***” means, with respect to a Licensed Product, the approval, agreement, determination or decision of any Regulatory Authority establishing the price or level of reimbursement for such Licensed Product, as applicable in a given country or jurisdiction prior to sale of such Licensed Product in such country or jurisdiction.

1.74“***Prosecute and Maintain***,” or “***Prosecution and Maintenance***,” with respect to a particular Patent, means all activities associated with the preparation, filing, prosecution and maintenance of such Patent.

1.75 “***Receiving Party***” has the meaning set forth in Section 8.1.1.

1.76“***Regulatory Approval***” means, collectively, any and all approvals (including supplements, amendments, pre- and post-approvals), licenses, registrations, permits, notifications, and authorizations (including marketing and labeling authorizations) or waivers of any Regulatory Authority that are necessary for the Research, Development, Manufacture, use or Commercialization of a pharmaceutical product (including any Licensed Product) in any country or jurisdiction, including Pricing and Reimbursement Approval, as applicable.

1.77“***Regulatory Authority***” means any Governmental Authority that has responsibility in its applicable jurisdiction over the Research, Development, Manufacture, use or Commercialization of pharmaceutical products (including any Licensed Product) in a given jurisdiction. For countries where governmental approval is required for pricing or reimbursement for a pharmaceutical product (including any Licensed Product) to be reimbursed by national health insurance (or its local equivalent), Regulatory Authority includes any Governmental Authority whose review or approval of pricing or reimbursement of such product is required.

1.78“***Regulatory Exclusivity***” means any rights or protections which are recognized, afforded or granted by the FDA or any other Regulatory Authority in the Territory pursuant to Applicable Laws, in association with the Marketing Authorization of the Licensed Product, providing the Licensed Product: (a) a period of marketing exclusivity, during which the Regulatory Authority recognizing, affording or granting such marketing exclusivity will refrain from either reviewing or approving a Marketing Authorization application or similar regulatory submission, submitted by a Third Party seeking to market a Generic Product of such Licensed Product, or (b) a period of data exclusivity, during which a Third Party seeking to market a Generic Product of such Licensed Product is precluded from either referencing or relying upon, without an express right of reference from the dossier holder, the Licensed Product’s clinical dossier or relying on previous regulatory authority findings of safety or effectiveness with respect to such Licensed Product to support the submission, review or approval of a Marketing Authorization application or similar regulatory submission before the applicable Regulatory Authority.

1.79“***Regulatory Filings***” means, collectively, any and all applications, filings, submissions, approvals (including supplements, amendments, pre- and post-approvals, pricing and reimbursement approvals), licenses, registrations, permits, notifications, and authorizations (including marketing and labeling authorizations) or waivers with respect to the Research, Development, Manufacture, use or Commercialization of a Licensed Product made to or received from any Regulatory Authority in a given country, including INDs.

1.80“***Relevant Date***” means the date on which [***] for the relevant Licensed Product.

1.81“***Research***” means any and all activities directed to discovery, identification, screening, testing, assessment and optimization of pharmaceutical compounds in advance of Development.

1.82 “***Royalty***” has the meaning set forth in Section 4.3.3.

1.83 “***Royalty Term***” has the meaning set forth in Section 4.3.1.

1.84 “***Sales Milestone Payment***” has the meaning set forth in Section 4.2.

1.85“***Sublicensee***” means a Third Party that is granted a license or sublicense or an option to obtain a license to sublicense to Research, Develop, Manufacture, use, Commercialize or otherwise exploit Licensed Products in the Field in the Territory, beyond the mere right to purchase Licensed Products from Fulcrum and its Affiliates, and excludes Fulcrum’s Affiliates or Third Party subcontractors that act solely for Fulcrum or its Affiliates in the supply chain or that perform discrete services (as opposed to being granted broad rights or responsibilities) on behalf of Fulcrum or its Affiliates.

1.86 “***Term***” has the meaning set forth in Section 9.1.

1.87 “***Territory***” means the entire world.

1.88 "***Third Party***" means a Person other than: (a) Fulcrum or its Affiliates; and (b) CAMP4 or its Affiliates.

1.89 "***Third Party Claim***" has the meaning set forth in Section 7.1.1.

1.90"***Third Party Distributor***" means any Third Party that purchases Licensed Product from Fulcrum or its Affiliates or Sublicensees, takes title to such Licensed Product, and distributes such Licensed Product directly to customers, but does not Develop, Manufacture, or otherwise Commercialize any Licensed Product and does not make any upfront, milestone, royalty, profit- share, or other payment to Fulcrum or its Affiliates or Sublicensees, other than payment for the purchase of Licensed Products for resale.

1.91"***Tier 1 Product***" means any product which on the Relevant Date is Covered by a Valid Claim of a CAMP4-Assignee Patent. For clarity, Tier 1 Products may or may not be Covered by a Valid Claim of a CMCC-Licensed Patent.

1.92"***Tier 2 Product***" means any product which on the Relevant Date is Covered by a Valid Claim of a CMCC-Licensed Patent, but is not Covered by a Valid Claim of a CAMP4- Assignee Patent.

1.93"***Transferred Materials***" has the meaning set forth in the CMCC License Agreement.

1.94 "***U.S.***" means the United States of America and its territories and possessions.

1.95 "***U.S. Approval***" means the grant of Marketing Authorization in the U.S.

1.96"***Valid Claim***" means (i) a claim of any issued, unexpired patent included within the Licensed Patents that has not been (a) held to be invalid, unenforceable or unpatentable by a final judgment of a court or other governmental authority of competent jurisdiction from which no appeal can be or is taken or (b) abandoned, disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise, or (ii) a claim of any pending patent application included within the Licensed Patents, which (a) patent application was filed and is being prosecuted in good faith and has not been cancelled, withdrawn from consideration, abandoned or finally disallowed without the possibility of appeal and (b) that has not been pending for [***] from the receipt of the first office action on the merits in the relevant patent office for such patent application; provided that if a claim issues after the time frame identified in clause (ii)(b) of this Section 1.96, and meets the requirements of clause (i) of this Section 1.96, such patent claim shall be deemed a Valid Claim upon issuance.

ARTICLE 2

LICENSE GRANT

2.1 **Grant of License**.

2.1.1**Exclusive License.** Subject to Section 2.4, CAMP4, on behalf of itself and its Affiliates, hereby grants to Fulcrum a worldwide, exclusive, royalty-bearing license, with the right to grant sublicenses (through multiple tiers, but only in accordance with Section 2.2), to and under the Licensed Patents and the CAMP4 Know-How, to Research, Develop, Manufacture, use, Commercialize, or otherwise exploit the Licensed Products in the Field in the Territory.

2.1.2**Non-Exclusive License.** CAMP4, on behalf of itself and its Affiliates, hereby grants to Fulcrum a non-exclusive license, with the right to grant sublicenses (through multiple tiers, but only in accordance with Section 2.2), to utilize or practice the CMCC Know- How and use the Transferred Materials to Research, Develop, Manufacture, use, Commercialize, or otherwise exploit the Licensed Products in the Field in the Territory.

2.2 **Sublicensing**.

2.2.1Fulcrum and its Affiliates may grant one or more sublicenses under the rights and licenses granted to Fulcrum under Section 2.1, in full or in part, to Third Parties (with the right to sublicense through multiple tiers); *provided*, *however*, that: (a) any sublicense of CMCC-Licensed Patents shall include an exclusive right to Develop or Commercialize a Licensed Product in a certain field or Major Market; (b) sublicenses of CMCC Know-How or Transferred Materials shall only be granted in connection with the sublicense of one or more CMCC-Licensed Patents, or to contractors for the purpose of carrying out the Development Plan or to a Third Party in connection with Licensed Products; (c) any such permitted sublicense is consistent with and subject to the terms and conditions of this Agreement; and (d) Fulcrum shall remain responsible for performance of Fulcrum’s obligations under this Agreement and shall be responsible for all actions of each such Sublicensee as if such Sublicensee were Fulcrum hereunder.

2.2.2Except with respect to sublicenses that grant rights to perform a service on behalf of Fulcrum, its Affiliates or Sublicensees (e.g. a contractor carrying out an activity under the Development Plan, or a contract manufacturer) under which Fulcrum, its Affiliates or Sublicensees do not receive any consideration other than the provision of services in exchange for rights granted under such sublicense, Fulcrum shall provide CAMP4 with notice of any grant of sublicense and a copy of fully executed sublicense agreements within [***] of execution thereof, which copy may be redacted to exclude information not relevant to the CMCC-Licensed Patents or CMCC Know-How.

2.3 **Maintenance of the CMCC License Agreement**. CAMP4 shall:

2.3.1not breach its obligations under the CMCC License Agreement in any material respect (except to the extent that any such breach is a result of any action or inaction by Fulcrum);

2.3.2comply in all respects with its obligations to bear the costs for the filing, prosecution or maintenance of the CMCC-Licensed Patents under Article VII of the CMCC License Agreement, *provided* that Fulcrum will reimburse CAMP4 for such costs in accordance with Section 5.1.3;

2.3.3not modify or amend the CMCC License Agreement in any way that would adversely affect Fulcrum or its rights hereunder in any material respect, without Fulcrum’s prior written consent, which shall not be unreasonably withheld, delayed or conditioned, and shall provide Fulcrum with a copy of all modifications to or amendments of the CMCC License Agreement;

2.3.4not terminate the CMCC License Agreement in whole or in part without Fulcrum's prior written consent;

2.3.5within [***] after CAMP4's knowledge thereof, provide Fulcrum with notice of and information relating to (i) any termination notice relating to the CMCC License Agreement, or (ii) any alleged material breach in writing by CAMP4 or CMCC of the CMCC License Agreement that would adversely affect in any material respect CAMP4 or Fulcrum or its rights hereunder or could reasonably give rise to a right to terminate the CMCC License Agreement and, following Fulcrum's request, reasonably consult with Fulcrum before taking any action in relation to such alleged or suspected breach or default (provided that CAMP4 shall have final say with respect to any such matter); and

2.3.6keep Fulcrum reasonably informed of any material developments under or relating to the CMCC License Agreement.

2.4**No Other Rights; Retained Rights**. Fulcrum acknowledges the reservations of rights in relation to the CMCC-Licensed Patents set forth in Article II B and C of the CMCC License Agreement. Except as set forth herein, neither Party shall be granted, by implication or otherwise any license or other intellectual property interest under any trademarks, Know-How, or Patents of the other Party.

2.5**Provision of Materials and Know-How**. To the extent not already provided to Fulcrum prior to the Effective Date, within [***] of the Effective Date, CAMP4 will provide Fulcrum with a copy of the Know-How listed in <u>Exhibit B</u> in a format and manner reasonably agreed by the Parties. On the request of Fulcrum, CAMP4 will ship to Fulcrum [***].

2.6 **Exclusivity**.

2.6.1Subject to Section 2.6.2, During the Term neither CAMP4, nor any of its Affiliates, will directly or indirectly, either alone or with or through one or more Third Parties, Research, Develop, Manufacture, use, Commercialize, or otherwise exploit [***] (a "***Competing Product***") in the Territory.

2.6.2CAMP4 will not be in breach of the restrictions set forth in Section 2.6.1 if CAMP4 or any of its Affiliates undergoes a Change of Control with a Third Party (together with such Third Party and its Affiliates following the closing of the applicable Change of Control transaction, the "***Acquired Party***") that (either directly or through an Affiliate (other than CAMP4 and any CAMP4 Affiliates that existing prior to such Change of Control), or in collaboration with any other Third Party) at the closing of the Change of Control transaction or thereafter is Researching, Developing, using, Commercializing or otherwise exploiting a Competing Product, as long as [***].

ARTICLE 3

DILIGENCE, DEVELOPMENT AND COMMERCIALIZATION

3.1**Diligence**. Fulcrum shall use Commercially Reasonable Efforts to obtain a Marketing Authorization for at least one Licensed Product in the Field in a Major Market. Without prejudice to the generality of the foregoing, Fulcrum shall use Commercially Reasonable Efforts to Research and Develop a Tier 1 Product. In the event that Fulcrum determines that a Tier 1 Product cannot be advanced despite the exercise of Commercially Reasonable Efforts, Fulcrum shall use Commercially Reasonable Efforts to Develop a Tier 2 Product. In the event that Fulcrum determines that a Tier 2 Product cannot be advanced despite the exercise of Commercially Reasonable Efforts, Fulcrum may terminate this Agreement in accordance with Section 9.6.

3.2**Development and Commercialization Responsibilities**. Subject to Section 3.1, all decisions concerning the Research, Development, Manufacture and Commercialization of the Licensed Product, including the clinical and regulatory strategy of the Licensed Product, the marketing and sales of the Licensed Product, and the design, price, and promotion of the Licensed Product, shall be at the sole discretion of Fulcrum. If Fulcrum reasonably requests assistance or input from CAMP4 with respect to Research or Development activities being undertaken by Fulcrum in respect of a Licensed Product, CAMP4 shall (at Fulcrum's expense), use its Commercially Reasonable Efforts to cooperate in good faith with Fulcrum in response to such request (e.g., by responding to regulatory inquiries relating to the pre-clinical development of a Licensed Product by CAMP4, intellectual property matters with respect to Licensed Patents and Know-How, etc.).

3.3**Reporting Obligations**. Fulcrum shall keep CAMP4 reasonably informed as to the progress and results of its and its Affiliates' and Sublicensees' Research and Development activities under this Agreement with respect to Licensed Products, including with respect to the achievement of Development Milestone Events. Fulcrum shall provide CAMP4: (a) copies of a high-level development plan ("***Development Plan***") in respect of Licensed Products [***] including [***]; the initial Development Plan is attached as Exhibit D and (b) reports, [***], with respect to material Research and Development activities undertaken by Fulcrum (including [***]) ("***Development Report***"). Fulcrum's reporting obligations under this Section 3.3 with respect to Fulcrum's Research and Development activities shall cease upon the achievement of all Development Milestone Events and Commercial Milestone Events in Table 4.2.1, after which time Fulcrum shall provide CAMP4 with reports as provided in Section 4.5, but Fulcrum shall have no additional reporting obligations with respect to its Commercialization activities.

3.4**CMCC Consent**. CAMP4 confirms that it has obtained and provided to Fulcrum a written confirmation signed by CMCC and CAMP4 that [***].

3.5**Regulatory Responsibilities**. Fulcrum shall be responsible for the preparation, submission, and maintenance of all Regulatory Filings and obtaining Regulatory Approvals (including the preparation and submission of the IND filing and for seeking IND approval) with respect to any Licensed Product and shall have sole control over all interactions with the applicable Regulatory Authority. CAMP4 shall reasonably cooperate with Fulcrum, at Fulcrum's reasonable request and expense, with respect to any regulatory matters related to any Licensed Product.

Fulcrum will own all right, title and interest in and to any and all Regulatory Filings and Regulatory Approvals for any Licensed Product and, as between the Parties, all such Regulatory Filings and Regulatory Approvals will be held in the name of Fulcrum, and CAMP4 shall execute all documents and take all actions as are necessary or reasonably requested by Fulcrum to vest such title in Fulcrum.

3.6**Compliance with Law; Export Controls**. Fulcrum shall comply with all applicable laws and regulations, including, without limitation, statutes and regulations affecting drug testing, development, marketing and distribution; laws and implementing regulations of the Department of Commerce governing intellectual property in federally-funded inventions; and Export Administration Regulations of the U.S. Department of Commerce issued pursuant to the Export Administration Act of 1979 (50 App. U.S.C. §2401 et. seq.). Fulcrum understands and acknowledges that transfer of certain technical data, computer software, laboratory prototypes and other commodities is subject to U.S. laws and regulations controlling their export, some of which prohibit or require a license for the export of certain types of technical data, to certain specified countries. CMCC has neither represented that a license shall not be required, nor that if required, it shall be issued. Fulcrum hereby represents and warrants that it will comply with all U.S. laws and regulations, and any applicable similar laws and regulations of any other country, controlling the export of commodities and technical data, that it will be responsible for any violation of such by Fulcrum or its Affiliates or Sublicensees, and that it will defend and hold CMCC, Harvard, DFCI, HHMI and their respective Affiliates and officers, directors, employees, agents, and medical staff harmless in the event of any Third Party legal action of any nature occasioned by such violation, and any action by any governmental agency or authority, relating to any asserted illegality or regulatory violation in the development, production, approval, marketing, sale, storage, manufacture, distribution, export or commercialization of Licensed Products by Fulcrum, its Affiliate or Sublicensee. It is the intention of the Parties hereto to comply with all applicable laws, rules, and regulations, including (i) the federal anti-kickback statute (42 U.S.C. §1320a-7b) and related safe harbor regulations, and (ii) the Limitation Certain Physician Referrals (42 U.S.C. §1395nn, the "Stark Law"). Accordingly, the Parties agree and acknowledge that no consideration received under this Agreement is, or is intended to be, a prohibited payment for the recommending or arranging for the referral of business or ordering of items or services, nor is any such consideration intended to induce illegal referrals of business.

ARTICLE 4

FEES, ROYALTIES, & PAYMENTS

4.1**Upfront Payment**. In consideration of the grant of rights by CAMP4 to Fulcrum on the Effective Date, Fulcrum shall pay to CAMP4 a non-refundable, non-creditable [***] within [***] after the Effective Date.

4.2 **Milestones**.

4.2.1**Milestone Payments**. Fulcrum shall pay to CAMP4 certain non-refundable and non-creditable milestone payments as follows. Where the Licensed Product is a Tier 1 Product, payments shall be made in the amounts indicated in the central column; where the Licensed Product is a Tier 2 Product, payments shall be made in the amounts indicated in the right hand column:

(a)within [***] following such Licensed Product achieving a development milestone event set forth in Table 4.2.1 below (each, a "***Development Milestone Event***"), Fulcrum shall pay to CAMP4 the relevant Milestone Payment indicated in Table 4.2.1 (each such Milestone Payment, a "***Development Milestone Payment***");

(b)within [***] following the end of the Calendar Quarter in which such Licensed Product achieves a commercial milestone event set forth in Table 4.2.1 (each, a "***Commercial Milestone Event***"), Fulcrum shall pay to CAMP4 the relevant Milestone Payment indicated in Table 4.2.1 (each such Milestone Payment, a "***Commercial Milestone Payment***"); and

(c)within [***] following the end of the Calendar Quarter in which any such Licensed Product achieves a sales milestone event set forth in Table 4.2.1 (each, a "***Sales Milestone Event***"), Fulcrum shall pay to CAMP4 the relevant Milestone Payment indicated in Table 4.2.1 (each such Milestone Payment, a "***Sales Milestone Payment***").

Table 4.2.1 – Development, Commercial and Sales Milestone Payments

Development Milestone Events	**Milestone Payment for Tier 1 Product**	**Milestone Payment for Tier 2 Product**
[***]	[***]	[***]
[***]	[***]	[***]

[***]	[***]	[***]
[***]	[***]	[***]
Commercial Milestone Events		
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
Sales Milestone Event		
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]

4.2.2**No Duplicate Milestone Payments**. Milestone Payments shall be payable only once per Milestone Event. For clarity, no Milestone Payment shall be payable for subsequent or repeated achievements of the same Milestone Event under with respect to the same or different Licensed Product or a different indication.

4.2.3**Milestone Payments Caps**. The maximum total amount payable by Fulcrum in respect of Tier 1 Products for all Development Milestone Payments shall not exceed [***]. The maximum total amount payable by Fulcrum in respect of Tier 1 Products for all Commercial Milestone Payments shall not exceed [***]. The maximum total amount payable by Fulcrum in respect of Tier 1 Products for all Sales Milestone Payments shall not exceed [***]. The maximum total amount payable by Fulcrum in respect of Tier 2 Products for all Development Milestone Payments shall not exceed [***]. The maximum total amount payable by Fulcrum in respect of Tier 2 Products for all Commercial Milestone Payments shall not exceed [***]. The maximum total amount payable by Fulcrum in respect of Tier 2 Products for all Sales Milestone Payments shall not exceed [***].

4.2.4**Satisfaction of Earlier Milestone Events**. The Development Milestone Events and Sales Milestone Events (but not the Commercial Milestone Events) are intended to be sequential, such that satisfaction of any later stage Milestone Event shall be deemed to have satisfied all earlier stage Milestone Events (to the extent not previously satisfied). Without prejudice to the generality of the foregoing: [***]

4.3 **Royalties on Licensed Products**.

4.3.1**Minimum Annual Royalty**. Fulcrum shall pay CAMP4 the following minimum annual royalty payments no later than [***] before [***], which will be creditable against Royalties paid in the same Calendar Year:

Year	Minimum Annual Royalty
[***]	[***]
[***]	[***]

[***]	[***]

Amounts owed pursuant to this Section 4.3.1 are fully creditable against Royalties due hereunder. If the Royalties paid in a Calendar Year do not exceed the minimum annual royalty paid under this Section 4.3.1, then Fulcrum may carry forward the unused amount and apply such amount against the Royalties owed to CAMP4 in subsequent Calendar Years until it is fully applied.

4.3.2**Royalty Term**. Subject to Section 4.4, Fulcrum shall pay CAMP4 royalties as set forth in this Section 4.3 on a Licensed Product-by-Licensed Product and country-by-country basis, shall commence with the First Commercial Sale of the Licensed Product in a country and continue until the later of: (a) the expiration of the last to expire Valid Claim Covering such Licensed Product in the country of sale, (b) ten (10) years from the date of the First Commercial Sale of such Licensed Product in such country, or (c) the expiration of Regulatory Exclusivity for such Licensed Product in such country (the "***Royalty Term***").

4.3.3**Royalty Rates**. On a Licensed Product-by-Licensed Product and country- by-country basis, during the Royalty Term, Fulcrum shall pay to CAMP4 a royalty equal to the percentages of annual Net Sales of such Licensed Product, as set forth in Table 4.3 below (the "***Royalty***"), as calculated by multiplying the applicable royalty percentage set forth in Table 4.3 below by the corresponding portion of aggregate Net Sales of all Tier 1 Products or Tier 2 Products, as applicable, in such Calendar Year.

<u>Table 4.3: Royalty Rates for Tier 1 Products and Tier 2 Products</u>.

Net Sales	**Royalty Rate for Tier 1 Product**	**Royalty Rate for Tier 2 Product**
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]

4.4 **Royalty Reductions**.

4.4.1**In General**. The royalty rates for Tier 2 Products are not subject to any reductions in the event of loss of patent coverage, generic entry, royalty stacking or otherwise. The royalty reductions under Sections 4.4.2, 4.4.3 and 4.4.4 only apply with respect to Tier 1 Products, and are subject to a [***] floor i.e. the royalty rate for a Tier 1 Product may not fall below the royalty rate for a Tier 2 Product shown in the right hand column of Table 4.3 even if more than one of Sections 4.4.2, 4.4.3 and 4.4.4 are applicable. By way of example, if annual global Net Sales of a given Tier 1 Product are less than [***], and the reduction set forth in Section 4.4.4 has operated to reduce the royalty rate from [***]% to [***]%, when there is no longer a Valid Claim Covering such Tier 1 Product the royalty rate shall only drop to [***]% for the remaining duration of the Royalty Term for such Tier 1 Product.

4.4.2**No Valid Claim**. In any Calendar Quarter during the Royalty Term for which there is no longer a Valid Claim of the CAMP4-Assignee Patents that Covers a given Tier 1 Product in a country, the Royalty rates provided in Section 4.3 for such Tier 1 Product will be reduced in such country by [***] for such Calendar Quarter.

4.4.3**Generic Products**. On a country-by-country and Tier 1 Product-by-Tier 1 Product basis from and after the first Calendar Quarter in which Generic Products with respect to a Tier 1 Product in any country in the Territory during the Royalty Term have a market share of [***] in a given country (measured in local currency, over the Calendar Quarter, as reported by [***]), the Royalty rates provided in Section 4.3 for the Tier 1 Product will be reduced in such country by [***].

4.4.4**Third Party Payments**. If it is reasonably required for Fulcrum to obtain a license or similar rights to a Patent of a Third Party in order for Fulcrum to develop, make, have made, use, sell, offer for sale and have sold, import, export and otherwise commercialize Tier 1 Products in the Field (a "***Third Party License***"), then Fulcrum shall have the right to credit [***] of any royalties actually paid by Fulcrum, its Affiliate or its Sublicensees under such Third Party License in a Calendar Quarter in respect of royalties in respect of such Tier 1 Product against the Royalties otherwise payable to CAMP4 under this Agreement for Tier 1 Products in such Calendar Quarter; provided that (a) Fulcrum may not deduct a greater percentage of royalties owed to a Third Party from Royalties due to CAMP4 than the percentage of royalties that Fulcrum is permitted to deduct from royalties owed to such Third Party pursuant to the royalty anti-stacking provision of such Third Party license and (b) the application of such credits shall not reduce the Royalties otherwise due to CAMP4 in any given Calendar Quarter by more than [***] (to reach the royalty floor of [***]) and any excess amounts that would have otherwise been deducted in such Calendar Quarter shall be deducted in successive Calendar Quarters until the credit has been realized in full.

4.5**Payment; Reports**. Royalty payments due by Fulcrum to CAMP4 under Section 4.3 will be calculated and reported for each Calendar Quarter. All Royalty payments due under Section 4.3 shall be paid [***] after the end of each Calendar Quarter and shall be accompanied by a report setting forth at least the following for each Licensed Product by Fulcrum and its Affiliates and Sublicensees in the Territory.

4.6**Method of Payment; Currency Conversion**. Unless otherwise agreed by the Parties, all payments due under this Agreement shall be paid in Dollars by wire transfer or electronic funds transfer of immediately available funds to an account designated by the payee; provided however, that Fulcrum shall only be required to disburse funds to the country containing payee's jurisdiction of incorporation or to a jurisdiction in which the payee has a significant business presence. When conversion of payments from any currency other than Dollars is required, Fulcrum's then-current standard exchange rate methodology will be employed for the translation of foreign currency sales into Dollars.

4.7**Records and Audits**. Fulcrum shall keep, and shall require its Affiliates and Sublicensees to keep full, true and accurate books and records, including books of account in accordance with GAAP, in sufficient detail to enable CAMP4 to determine Fulcrum's compliance with this Agreement, including diligence with respect to development as set forth in Section 3.1 and the royalty and other amounts payable to CAMP4 under this Agreement. Said books and records, including books of account in accordance with GAAP, shall be kept at Fulcrum's principal place of business or the principal place of business of the appropriate division of Fulcrum to which this Agreement relates. Said books of Fulcrum and Affiliates and the supporting data shall be retained for at least [***] following the end of the calendar year to which they pertain or such longer period as required by applicable law, rule or regulation. Fulcrum shall require its Sublicensees to retain such books and data for [***] following the end of the calendar year to which they pertain or such longer period as required by applicable law, rule or regulation and shall use [***] to require a [***] retention period from its Sublicensees. During the Term, CAMP4 shall not more than [***] have the right to have Fulcrum's then-current auditors inspect Fulcrum's records for the purpose of determining the accuracy of Royalty payments for a period covering not more than [***] following the Calendar Quarter to which they pertain. No period will be audited more than [***] and each audit must be reasonable in scope. The independent, certified public accountant selected shall keep confidential any information obtained during such inspection and shall report to CAMP4 and Fulcrum only the amounts of Net Sales and Royalties due and payable. Such audits may be exercised during normal business hours upon reasonable prior written notice to Fulcrum. [***] cost of such audit unless such audit discloses an underpayment by Fulcrum of [***], of the amount of Royalties or other payments due under this Agreement for any applicable Calendar Quarter, in which case, [***] cost of such audit and [***] of the date the auditor's written report is received. Any overpayment by Fulcrum revealed by an audit shall be [***].

4.8**Late Payments**. If any payment due under this Agreement is not paid when due in accordance with the applicable provisions of this Agreement, the payment shall accrue interest from [***] at the rate of [***] or the maximum rate allowable by Applicable Law, whichever is

[***]. The payment of such interest shall not limit the Party entitled to receive payment from exercising any other rights it may have as a consequence of the lateness of any payment.

4.9 **Taxes**

4.9.1**Cooperation and Coordination**. The Parties acknowledge and agree that it is their mutual objective and intent to minimize, to the extent feasible and in compliance with Applicable Laws, taxes payable with respect to their collaborative efforts under this Agreement and that they shall use reasonable efforts to cooperate and coordinate with each other to achieve such objective.

4.9.2**Payment of Tax**. The upfront, milestones, Royalties and other amounts payable by Fulcrum to CAMP4 under this Agreement (each, a "***Payment***") shall be [***].

4.10**Assignment of Rights to Milestone Payments and Royalties**. CAMP4 may assign its rights to Milestone Payments and Royalty payments to a Third Party (but not more than one Third Party at any given time during the Term); provided, that in no event shall Fulcrum be required to make Milestone Payments or Royalty payments to more than one Person (including CAMP4) and in no event shall such assignment affect the currency in which payments are to be made, payment terms, tax responsibilities or other financial obligations of Fulcrum.

ARTICLE 5

INTELLECTUAL PROPERTY

5.1 **Patent Prosecution and Maintenance**.

5.1.1**CAMP4-Assignee Patents**. Fulcrum shall have control over Prosecution and Maintenance of the CAMP4-Assignee Patents [***], provided that Fulcrum shall notify CAMP4 of its intention to suspend or cease any Prosecution and Maintenance of any Licensed Patent and provide such notice no less than [***] prior to any filing or payment due date, or any other due date that requires action, in connection with such Licensed Patent. In such event, Fulcrum shall permit CAMP4, at CAMP4's discretion [***], to continue Prosecution and Maintenance of such Licensed Patent.

5.1.2**CMCC-Licensed Patents**. Fulcrum acknowledges that, pursuant to the terms of the CMCC License Agreement, CMCC has the primary responsibility for the Prosecution and Maintenance of the CMCC-Licensed Patents. To the extent to which CAMP4 has the right under the CMCC License Agreement to provide input into the Prosecution and Maintenance of the CMCC-Licensed Patents, CAMP4 shall permit Fulcrum to exercise such rights on CAMP4's behalf. Without limitation to the generality of the foregoing, CAMP4 shall promptly share with Fulcrum the information that CAMP4 receives pursuant to Article VII of the CMCC License Agreement, shall provide Fulcrum with reasonable opportunity to comment on the Prosecution and Maintenance of the CMCC-Licensed Patents, shall share Fulcrum's comments with CMCC's patent counsel or arrange for Fulcrum to communicate directly with CMCC's patent counsel, and act in accordance with Fulcrum's instructions as regards any decision to no longer pay the expenses of Prosecuting and Maintaining any CMCC-Licensed Patent. In the event that CMCC elects not to Prosecute and Maintain a CMCC-Licensed Patent, CAMP4 shall promptly notify Fulcrum of any notifications it receives from CMCC pursuant to Article VII C of the CMCC License Agreement, and follow Fulcrum's directions as to whether or not to assume Prosecution and Maintenance of such CMCC-Licensed Patent. CAMP4 shall permit Fulcrum to exercise, at Fulcrum's discretion, CAMP4's step-in rights under Article VII C of the CMCC License Agreement.

5.1.3**Costs of Prosecuting CMCC-Licensed Patents**. As between the Parties, Fulcrum will be responsible for the costs of preparation, filing, prosecution, and maintenance of the CMCC-Licensed Patents during the Term. During the Term, CAMP4 will invoice Fulcrum for payments made by CAMP4 to CMCC pursuant to Article IV A 2 of the CMCC License Agreement and Fulcrum will pay each such invoice no later than [***].

5.2 **Infringement or Misappropriation by Third Parties**.

5.2.1**Notice**. Each Party shall notify the other within [***] of becoming aware of any alleged or threatened infringement by a Third Party of any of the Licensed Patents, which infringing activity involves the using, making, importing, offering for sale, or selling a Licensed Product or compound, product or therapy competitive to a Licensed Product, in each case in the Field in the Territory, and any related declaratory judgment, opposition, or similar action alleging the invalidity, unenforceability or non-infringement of any of the Licensed Patents (collectively "***Infringement***").

5.2.2**Control of Infringement Actions**. Subject to CMCC's rights in Article VIII of the CMCC License Agreement for CMCC-Licensed Patents, Fulcrum shall have the first right to bring and control any legal action in connection with any Infringement of any Licensed Patent at its own expense. Fulcrum shall keep CAMP4 reasonably informed of the status of such enforcement efforts for such Licensed Patent and shall consider in good faith CAMP4's comments thereon. CAMP4 may, at its own expense, be represented in any such action by counsel of its own choice. If Fulcrum does not exercise its right to bring or defend proceedings or otherwise take diligent and reasonable steps to abate the actual or suspected Infringement or challenge to a Licensed Patent within (a) [***] of the written notification pursuant to Section 5.2.1, (b) [***] before the time limit, or (c) [***] then CAMP4 may bring and control any legal action in connection with such Infringement of such Licensed Patent at its own expense as it reasonably determines appropriate so long as Fulcrum does not reasonably object to such action.

5.2.3**Allocation of Recoveries**. Any recoveries resulting from an enforcement action relating to a claim of Infringement shall be first paid, to the extent such recoveries are allocable to [***], and then applied against payment of each Party's costs and expenses in connection therewith. Any remaining recoveries will then be allocated [***] to the enforcing Party and [***] to the non-enforcing Party.

5.2.4**Cooperation**. At the request and expense of the Party controlling an action under this Section 5.2, the other Party shall provide reasonable assistance in connection therewith, including by executing reasonably appropriate documents, cooperating in discovery and joining as a party to the action if required by Applicable Law to pursue such action. CAMP4 shall, [***]. In connection with any such enforcement action, the Party bringing the action shall not enter into any settlement admitting (a) the invalidity or non-infringement of, or otherwise impairing the other Party's rights in the applicable Licensed Patents, (b) imposes any financial liability or other obligation on the part of the other Party, or (c) requires an admission of liability, wrongdoing or fault or a waiver of rights on the part of the other Party, without the prior written consent of the other Party.

ARTICLE 6

REPRESENTATIONS, WARRANTIES AND COVENANTS

6.1**Mutual Representations and Warranties**. Each of Fulcrum and CAMP4 represents and warrants, as of the Effective Date, that:

6.1.1it is duly organized and validly existing under in the Applicable Laws of the jurisdiction of its incorporation or formation, as applicable, and has full corporate, limited liability company or other power and authority, as applicable, to enter into this Agreement;

6.1.2it is duly authorized to execute and deliver this Agreement and to perform its obligations hereunder, and the individual executing this Agreement on its behalf has been duly authorized to do so by all requisite corporate, limited liability company or other action, as applicable; and

6.1.3this Agreement is legally binding upon it and enforceable in accordance with its terms (except as the enforceability thereof may be limited by bankruptcy, bank moratorium or similar laws affecting creditors' rights generally and laws restricting the availability of equitable remedies and may be subject to general principles of equity whether or not such enforceability is considered in a proceeding at law or in equity) and the execution, delivery and performance of this Agreement by it have been duly authorized by all necessary corporate action and do not and will not: (a) conflict with, or constitute a default or result in a breach under, any agreement, instrument or understanding, oral or written, to which it is a party or by which it may be bound, or violate any Applicable Law; or (b) require any consent or approval of its stockholders or similar.

6.2**CAMP4 Representations and Warranties**. CAMP4 represents and warrants to Fulcrum that, as of the Effective Date:

6.2.1**No Grants that Conflict with this Agreement**. CAMP4 and its Affiliates have not granted any rights (or other encumbrances) to any Third Party to the Licensed Patents, CMCC Know-How or CAMP4 Know-How that prevent or conflict with the rights granted to Fulcrum hereunder.

6.2.2**Control over Know-How and Licensed Patents**. The CAMP4 Know- How, CMCC Know-How and Licensed Patents include all Know-How and Patents owned or licensed by CAMP4 as of the Effective Date, that are necessary or reasonably useful for the Research, Development, Manufacturing, use or Commercialization of the Licensed Products as known by CAMP4 as contemplated by this Agreement as of the Effective Date.

6.2.3 **Licensed Patents**.

(a)The CAMP4-Assignee Patents are solely and exclusively owned by CAMP4, free of any encumbrance, lien or claim of ownership by any Third Party, and the CMCC- Licensed Patents are licensed to CAMP4 pursuant to the terms of the CMCC License Agreement;

(b)All Licensed Patents existing as of the Effective Date that are issued or subject to a pending application for issuance are listed on Exhibit A and all such Licensed Patents are, to CAMP4's knowledge: (i) to the extent issued (unless otherwise indicated on Exhibit A), subsisting and not invalid or unenforceable, in whole or in part; (ii) to the extent subject to a pending application for issuance, being diligently prosecuted in the respective patent offices in which such applications have been filed in accordance with Applicable Law and all relevant references, documents and information have been presented to the relevant patent examiner at the relevant patent office; and (iii) filed and maintained properly and correctly, and all applicable fees applicable thereto have been paid on or before the due date for payment.

(c)To CAMP4's knowledge, no owner of a Licensed Patent has taken any action that would render any invention claimed in the Licensed Patents unpatentable.

6.2.4 **Litigation and Actions Relating to Intellectual Property**. CAMP4: (a) has not received any written notice of any threatened claims or litigation seeking to invalidate or otherwise challenge the Licensed Patents, or CMCC, Harvard, DFCI, CAMP4's or its Affiliates' rights therein; (b) is not aware of any pending or threatened action, suit, proceeding or claim by a Third Party asserting that the practice of the Licensed Patents, CMCC Know-How or CAMP4 Know-How infringes or misappropriate or otherwise violates any Patent right, trade secret or other proprietary right of any Third Party; and (c) is not aware of any Patent right, trade secret or other proprietary right of any Third Party that would be infringed, misappropriated or otherwise violated by the future making, using, selling, importing or exporting of a Licensed Product under this Agreement.

6.2.5**Other Material Claims and Actions**. There are no claims, actions, or proceedings pending or, to CAMP4's knowledge, threatened by any Third Party; nor, to CAMP4's knowledge, are there any formal inquiries initiated or written notices received that may lead to the institution of any such legal proceedings, in each case (or in aggregate) against CAMP4 or its properties, assets or business, which if adversely decided, would, individually or in the aggregate, have a material adverse effect on, or prevent CAMP4's ability to grant the licenses or rights granted to Fulcrum under this Agreement.

6.2.6**No Government Funding for Licensed Patents**. The inventions that consist of or are claimed in the CAMP4-Assignee Patents: (a) were not conceived of, discovered, developed or otherwise made in connection with any research activities funded, in whole or in part, by the federal government of the United States of America or any agency thereof; (b) are not a "subject invention" as that term is described in 35 U.S.C. Section 201(e) and (c) are not otherwise subject to the provisions of the Patent and Trademark Law Amendments Act of 1980, as amended, codified at 35 U.S.C. §§ 200-212, as amended, as well as any regulations promulgated pursuant thereto, including in 37 C.F.R. Part 401.

6.3**Covenants of CAMP4**. CAMP4 and its Affiliates will not grant any rights (or other encumbrances) to any Third Party to the Licensed Patents, CMCC Know-How or CAMP4 Know-How that prevent or conflict with the rights granted to Fulcrum hereunder.

6.4**Disclaimer**. EXCEPT AS OTHERWISE EXPRESSLY SET FORTH IN THIS Article 6, NEITHER PARTY MAKES ANY REPRESENTATIONS OR EXTENDS ANY

WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY, QUALITY, FITNESS FOR A PARTICULAR PURPOSE, NONINFRINGEMENT, OR VALIDITY OF PATENT CLAIMS.

ARTICLE 7

INDEMNIFICATION

7.1 **Indemnity**.

7.1.1**By Fulcrum**. Fulcrum shall indemnify, defend and hold harmless CMCC, Harvard, DFCI and their respective Affiliates, current or future directors, trustees, officers, faculty, medical and professional staff, employees, students and agents and their respective successors, heirs and assigns, other than persons who are employees of HHMI, (the "CMCC ***Indemnitees***"), against any claim, liability, cost, damage, deficiency, loss, expense or obligation of any kind or nature (including without limitation reasonable attorneys' fees and other costs and expenses of litigation) ("***Losses***") incurred by or imposed upon the CMCC Indemnitees or any one of them in connection with any claim, demand, action or other proceeding by any Third Party (a "***Third Party Claim***") arising out of (i) any theory of product liability (including, but not limited to, actions in the form of tort, warranty, or strict liability) concerning any product, process or service made, used or sold by Fulcrum, its Affiliates, Sublicensees or its authorized agents pursuant to any right or license granted under this Agreement, or (ii) the use, handling, storage or disposition of the Transferred Material by Fulcrum, its Affiliates, Sublicensees or others who possess the Transferred Material through a chain of possession leading back, directly or indirectly, to Fulcrum.

7.1.2Fulcrum's indemnification under Section 7.1.1 above shall not apply to any Loss to the extent that it is attributable to the negligent activities, recklessness or intentional misconduct of the CMCC Indemnitees or breach of an obligation by CMCC under the CMCC License Agreement.

7.1.3CAMP4 shall, and shall cause any CMCC Indemnitee to, permit Fulcrum to have control of the defense of any actions brought or filed against a CMCC Indemnitee that are subject to the indemnification obligations of Fulcrum contained in this Agreement so long as Fulcrum promptly assumes the defense and prosecutes the defense with appropriate diligence and care and selects attorneys reasonably acceptable the CMCC Indemnitee, to defend such actions, provided however, that Fulcrum shall not admit any fault, liability or culpability on the part of CMCC Indemnitee without the prior written permission of such CMCC Indemnitee.

7.1.4HHMI and its trustees, officers, employees, and agents (collectively, "***HHMI Indemnitees***"), will be indemnified, defended by counsel reasonably acceptable to HHMI, and held harmless by Fulcrum from and against any claim, liability, cost, expense, damage, deficiency, loss, or obligation, of any kind or nature (including, without limitation, reasonable attorneys' fees and other costs and expenses of defense) (collectively, "***Claims***"), based upon, arising out of or otherwise relating to this Agreement or any sublicense, or the use, handling, storage, or disposition of the Transferred Material by Fulcrum, its Affiliates, Sublicensees or others who possess the Transferred Material through a chain of possession leading back, directly or indirectly, to Fulcrum, including without limitation any cause of action relating to product liability. The previous sentence will not apply to any Claim that is determined with finality by a court of competent jurisdiction to result solely from the gross negligence or willful misconduct of an HHMI Indemnitee. Notwithstanding any other provision of this Agreement, Fulcrum's obligation to defend, indemnify and hold harmless the HHMI Indemnitees under this paragraph will not be subject to any limitation or exclusion of liability or damages or otherwise limited in any way.

7.1.5**By CAMP4**. CAMP4 shall defend, indemnify and hold harmless Fulcrum and its Affiliates, and their respective directors, officers, employees, and agents (each, a "***Fulcrum Indemnitee***") from and against any and all Losses to which any Fulcrum Indemnitee may become subject as a result of any Third Party Claim to the extent such Losses arise out of: (a) the fraud, gross negligence or willful misconduct of CAMP4 or its Affiliates in connection with its activities under this Agreement; or (b) the breach of this Agreement or the representations, warranties, and covenants made hereunder by CAMP4, except, in each case, to the extent such Losses result from matters subject to clause (a), (b), or (c) of Section 7.1.6.

7.1.6**By Fulcrum**. Fulcrum shall defend, indemnify and hold harmless CAMP4, its Affiliates, and their respective directors, officers, employees and agents (each, an "***CAMP4 Indemnitee***") from and against any and all Losses to which any CAMP4 Indemnitee may become subject as a result of any Third Party Claim to the extent such Losses arise out of: (a) the fraud, gross negligence or willful misconduct of Fulcrum, its Affiliates, or their respective Sublicensees in connection with its activities under this Agreement; (b) the breach of this Agreement or the representations, warranties and covenants made hereunder by Fulcrum; or (c) the exploitation of Licensed Products by Fulcrum, its Affiliates, its authorized agents, or its Sublicensees, except, in each case, to the extent such Losses result from matters subject to clause (a) or (b) of Section 7.1.5.

7.1.7**Procedure**. A Party that intends to claim indemnification under this Article 7 (the "***Indemnitee***") shall promptly notify the Indemnitor (the "***Indemnitor***") in writing of any Third Party Claim in respect of which the Indemnitee intends to claim such indemnification. The failure to deliver written notice to the Indemnitor within a reasonable time after the commencement of any action with respect to a Third Party Claim shall only relieve the Indemnitor of its indemnification obligations under this Article 7 if and to the extent the Indemnitor is actually and materially prejudiced thereby. The Indemnitor has sole control of the defense or settlement thereof. The Indemnitee shall cooperate fully with the Indemnitor and its legal representatives in the investigation of any action with respect to a Third Party Claim covered by this indemnification. The Indemnitee may participate at its expense in the Indemnitor's defense of and settlement negotiations for any Third Party Claim with counsel of the Indemnitee's own selection. The Indemnitor shall not settle any Third Party Claim without the prior written consent of the Indemnitee, not to be unreasonably withheld. So long as the Indemnitor is actively defending the Third Party Claim in good faith, the Indemnitee shall not settle or compromise any such Third Party Claim without the prior written consent of the Indemnitor. If the Indemnitor does not assume and conduct the defense of the Third Party Claim as provided above: (a) the Indemnitee may defend against, consent to the entry of any judgment, or enter into any settlement with respect to such Third Party Claim in any manner the Indemnitee may deem reasonably appropriate (and the Indemnitee need not consult with, or obtain any consent from, the Indemnitor in connection therewith); and (b) the Indemnitor shall remain responsible to indemnify the Indemnitee as provided in this Article 7.

7.2**Insurance**. Beginning at the time as any such product, process or service is being commercially distributed or sold (other than for the purpose of obtaining regulatory approvals) by Fulcrum or by a Sublicensee, Affiliate or an authorized agent of Fulcrum, Fulcrum shall, at its sole cost and expense, procure and maintain commercial general liability insurance in amounts not less than [***] and naming the CAMP4 Indemnitees and HHMI Indemnitees as additional insureds. Such commercial general liability insurance shall provide (i) product liability coverage and (ii) contractual liability coverage for Fulcrum's indemnification under this Article 7. [***] The minimum amount of insurance coverage required under this Section 7.2, shall not be construed to create a limit of Fulcrum's liability with respect to its indemnification under Article 7 of this Agreement. Fulcrum shall provide CAMP4 with written evidence of such insurance upon request of CAMP4. Fulcrum shall provide CAMP4 with written notice at least [***] prior to the cancellation, non-renewal or material change in such insurance. Notwithstanding any other term of this Agreement, if Fulcrum does not obtain replacement insurance providing comparable coverage prior to the cancellation or non-renewal of such insurance, CAMP4 shall have the right to terminate this Agreement effective at the end of such [***] without notice of any additional waiting periods. Fulcrum shall maintain such commercial general liability insurance during [***].

7.3**Survival**. The provisions of this Article 7 survive expiration or termination of this Agreement.

ARTICLE 8

CONFIDENTIALITY

8.1 **Confidential Information**.

8.1.1**Restrictions**. A Party (the "***Receiving Party***") that receives Confidential Information from the other Party (the "***Disclosing Party***") under this Agreement shall keep all the Disclosing Party's Confidential Information in confidence with the same degree of care with which the Receiving Party holds its own confidential information (but in no event less than a commercially reasonable degree of care). A Receiving Party shall not use the Disclosing Party's Confidential Information except in connection with the performance of its obligations and exercise of its rights under this Agreement, or as permitted under Section 8.1.2.

8.1.2**Exceptions**. The obligations of confidentiality and restriction on use of Confidential Information under Section 8.1.1 do not apply to any information that the Receiving Party can prove by competent written evidence: (a) is now, or hereafter becomes, through no act or failure to act on the part of the Receiving Party, generally known or available to the public;
(b) is known by the Receiving Party at the time of receiving such information, other than by previous disclosure of the Disclosing Party, or its Affiliates, employees, agents, consultants, or contractors; (c) is hereafter furnished to the Receiving Party without restriction by a Third Party who has no obligation of confidentiality or limitations on use with respect thereto, as a matter of right; or (d) is independently discovered or developed by the Receiving Party without the use of Confidential Information belonging to the Disclosing Party. Specific information shall not be deemed to be within any of the foregoing exclusions merely because it is embraced by more general information falling within those exclusions.

8.1.3**Permitted Disclosures**. The Receiving Party may disclose Confidential Information belonging to the Disclosing Party as expressly permitted by this Agreement or if and to the extent such disclosure is reasonably necessary in the following instances:

(a) Prosecution and Maintenance of Patents as permitted by this Agreement;

(b) Regulatory Filings for Licensed Product that such Party has a license or right to develop hereunder in a given country or jurisdiction;

(c) prosecuting or defending litigation as permitted by this Agreement;

(d) complying with applicable court orders or governmental regulations, including mutually recognized securities laws;

(e) in response to a valid request by a U.S., state, foreign, provincial, or local tax authority, in which case either Party may disclose, a copy of this Agreement (including any Exhibits, schedules, ancillary agreements, and amendments hereto);

(f) disclosure to its and its Affiliates' employees, consultants, contractors and agents, and to Sublicensees (in the case of Fulcrum), in each case on a need-to- know basis in connection with the Research, Development, Manufacture, use, Commercialization, or other exploitation of Licensed Products in accordance with the terms of this Agreement, in each case under written obligations of confidentiality and non-use; and

(g) disclosure to potential and actual investors, acquirers, licensees and other financial partners solely for the purpose of evaluating or carrying out an actual or potential investment, acquisition or financing, in each case under written obligations of confidentiality and non-use at least as stringent as those herein; *provided*, *however*, that with respect to disclosure to actual or bona fide potential investors or financiers, such disclosure is under a written obligation of confidentiality that is consistent with market terms, including a shorter period of time during which such information must be held confidential.

Notwithstanding the foregoing, if a Party is required to make a disclosure of the other Party's Confidential Information pursuant to Section 8.1.3(d) or (e), it shall, except where impracticable, give reasonable advance notice to the other Party of such disclosure and use efforts to secure confidential treatment of such Confidential Information at least as diligent as such Party would use to protect its own Confidential Information, but in no event less than reasonable efforts. Any information disclosed pursuant to Section 8.1.3(d) or (e) remains Confidential Information and subject to the restrictions set forth in this Agreement, including the foregoing provisions of this Article 8.

8.1.4 **Disclosure of Agreement**. Notwithstanding the foregoing, either Party or its Affiliates may disclose the relevant terms of this Agreement: (a) to the extent required or advisable to comply with the rules and regulations promulgated by the U.S. Securities and Exchange Commission or any equivalent governmental agency or the rules of any recognized stock exchange in any country in the Territory, provided that such Party shall submit a confidential treatment request in connection with such disclosure and shall submit with such confidential treatment request only such redacted form of this Agreement as may be mutually agreed in writing by the Parties; (b) upon request from a Governmental Authority (such as a tax authority), provided the disclosing Party uses reasonable efforts to ensure the Governmental Authority maintains such terms as confidential; (c) to CMCC, to the extent necessary to comply with the terms of the CMCC License Agreement; (d) to potential and actual investors, acquirers, licensees and other financial partners solely for the purpose of evaluating or carrying out an actual or potential investment or acquisition, in each case under written obligations of confidentiality and non-use at least as stringent as those herein; *provided*, *however*, that with respect to disclosure to actual or bona fide potential investors, such disclosure is under a written obligation of confidentiality that is consistent with market terms, including a shorter period of time during which such information must be held confidential; and (e) (in the case of Fulcrum) to the extent necessary in connection with the performance of obligations or exercise of rights under this Agreement, to any Sublicensee, collaborator or potential Sublicensee or potential collaborator, *provided however* such Person agrees in writing to be bound by obligations of confidentiality and non-use no less protective of the Disclosing Party than those set forth in this Agreement.

8.1.5**Survival**. Each Party's obligations with respect to Confidential Information under this Section 8.1 apply during the Term and continue for [***] thereafter.

8.2**Publicity**. CAMP4 acknowledges that Fulcrum is a publicly traded company and that the disclosure of non-public information regarding Fulcrum or trading in the securities of Fulcrum while in the possession of such information may, depending on the facts and circumstances, subject CAMP4 to liability under the regulations or the rules of the U.S. Securities and Exchange Commission, NASDAQ or any stock exchange on which Fulcrum's shares are listed or the U.S. Securities and Exchange Act of 1934, as amended. Fulcrum shall issue a press release in the form attached hereto as Exhibit C promptly after the Effective Date. Thereafter, either Party may make subsequent public disclosure of the contents of such press release. Except as permitted under Section 8.1.3 and this section 8.2, neither Party shall issue any subsequent press release or public statement disclosing information relating to this Agreement or the transactions contemplated hereby or the terms hereof without the prior written consent of the other Party, not to be unreasonably withheld, conditioned, or delayed; provided however, that neither Party will not be prevented from (i) complying with any duty of disclosure it may have pursuant to Applicable Laws or pursuant to the rules of any recognized stock exchange, or (ii) repeating any information relating to this Agreement that has already been publicly disclosed by the other Party.

8.3**Proprietary, Non-Public Information**. Fulcrum hereby covenants and agrees that it will not use or cause to be used proprietary, non-public information that CAMP4 has acquired from CMCC or any Affiliate thereof in the course of prosecution of the CMCC-Licensed Patents, or patent counsel prosecuting the CMCC-Licensed Patents on behalf of Fulcrum or its Affiliates and such information shall be considered Confidential Information of CMCC or its Affiliates and be subject to CAMP4's obligations under Article VI of the CMCC License Agreement. But for satisfying Fulcrum's obligations under 37 CFR 1.56 and any other similar statutory, regulatory or professional ethical requirement, Fulcrum shall not advise counsel prosecuting such CMCC- Licensed Patents to include information in any such patent application that would, to Fulcrum's knowledge, have a material, negative impact on CMCC's or its Affiliate's ownership of such rights or the validity of such CMCC-Licensed Patents. Any assignment or sublicense granted by Fulcrum shall contain an identical commitment by the assignee or Sublicensee.

ARTICLE 9

TERM & TERMINATION

9.1**Term**. This Agreement commences on the Effective Date and, unless terminated earlier as provided in accordance with this Agreement, shall continue on a Licensed Product-by- Licensed Product basis until the expiration of the Royalty Term in the Territory for such Licensed Product (the "***Term***"). Upon the expiration of the Royalty Term for a Licensed Product in a particular country, the licenses granted by CAMP4 to Fulcrum under Section 2.1 with respect to such Licensed Product and such country shall survive and become perpetual, fully-paid, and royalty-free, and shall remain exclusive (even as to CAMP4 and its Affiliates).

9.2**Termination for Failure to Pay**. CAMP4 may terminate this Agreement upon [***] prior written notice in the event of Fulcrum's failure to pay to CAMP4 any amounts properly due and payable hereunder in a timely manner, unless Fulcrum shall make all such payments to CAMP4 within said [***]; provided that the cure period will be tolled pending resolution of any bona fide dispute between the Parties as to whether such payments is due and payable under this Agreement. Upon the expiration of the [***] (plus any additional time due to tolling of the cure period), if Fulcrum shall not have made all such undisputed payments to CAMP4, the rights, privileges and licenses granted hereunder shall terminate without further action by CAMP4.

9.3**Termination for Patent Challenge**. CAMP4 may terminate this Agreement upon [***] written notice to Fulcrum if Fulcrum or Fulcrum's Affiliate, or Sublicensee takes actions to challenge, in a judicial or administrative proceeding, the validity of any CMCC-Licensed Patent, provided that Fulcrum has not revoked or caused to be revoked such proceeding within [***]; provided further that the foregoing right to terminate shall not apply where such challenge of a CMCC-Licensed Patent is the assertion of a defense or counterclaim to an action first brought by CMCC against Fulcrum. For the avoidance of doubt, any participation by Fulcrum, its Affiliate, Sublicensee or any of their respective employees in any claim, challenge or proceeding in response to a subpoena shall not constitute an active challenge and shall not give rise to CAMP4's right to terminate this Agreement.

9.4**Termination for Material Breach**. Either Party may terminate this Agreement, upon written notice to the other Party if such other Party materially breaches its obligations under this Agreement and, after receiving written notice from the non-breaching Party identifying such material breach in reasonable detail, fails to cure such material breach within [***] from the date of such notice; *provided* that if such breach is not reasonably capable of cure within [***], the breaching Party may submit, prior to the end of [***], a reasonable plan to cure the breach within [***] in which case the other Party may not terminate this Agreement for so long as the breaching Party is [***] to implement such cure plan within [***].

9.5**Termination for Insolvency**. A Party may immediately terminate this Agreement upon written notice to the other Party if such other Party becomes insolvent or is unable to pay its debts as they become due, makes an assignment for the benefit of its creditors, enters into bankruptcy or similar proceedings, or has a receiver or custodian appointed for it, or ceases to conduct business or enters into dissolution or liquidation proceedings.

9.6**Termination by Fulcrum without Cause**. Fulcrum may, in its sole discretion, terminate this Agreement in its entirety at any time and without cause [***] prior written notice to CAMP4.

9.7**Disputed Breach**. If the allegedly breaching Party disputes in good faith the existence or materiality of a breach specified in a notice provided by the other Party in accordance with Section 9.4, and such allegedly breaching Party provides the other Party notice of such dispute within [***] then the non-breaching Party may not terminate this Agreement under Section 9.4 unless and until it has been finally determined pursuant to Article 10 that the alleged breaching Party has materially breached this Agreement and such Party fails to cure such breach within [***] following a final and non-appealable court decision. During the pendency of such dispute, all of the terms and conditions of this Agreement shall remain in effect and the Parties shall continue to perform all of their respective obligations hereunder.

9.8 **Effects of Termination**.

9.8.1**Termination of Licenses**. All licenses for Licensed Products granted under Section 2.1 terminate automatically as of the termination effective date; provided that, if Fulcrum (or its Affiliates or Sublicensees) has inventory of usable Licensed Product(s) as of the effective date of termination, then Fulcrum (and its Affiliates and Sublicensees) may continue to sell off such inventory of Licensed Products in the Field in the Territory (and fulfill customer orders therefor) until [***], and shall pay CAMP4 any applicable Royalties due based on such sales. Notwithstanding the foregoing, upon termination of this Agreement for any reason, upon the request of any Sublicensee of Fulcrum who is not then in breach of its sublicense agreement or the terms and conditions of this Agreement applicable to such Sublicensee, CAMP4 will enter into a direct license to such Sublicensee on the same terms as this Agreement, taking into account any difference in license scope, territory and duration of sublicense grant (each a “***New License Agreement***”). Under any such New License Agreement between CAMP4 and such former Sublicensee, (a) such former Sublicensee will be required to pay to CAMP4 the same amounts in consideration for such direct grant as CAMP4 would have otherwise received from Fulcrum pursuant to this Agreement on account of such former Sublicensee’s exploitation of the Licensed Products had this Agreement not been terminated and (b) CAMP4 will not be bound by any grant of rights broader than, and will not be required to perform any obligation other than those rights and obligations contained in, this Agreement.

9.8.2**Destruction of Confidential Information**. Each Receiving Party shall destroy (at the Disclosing Party’s written request) all such Confidential Information of the Receiving Party in its possession as of the effective date of expiration or termination (with the exception of one copy of such Confidential Information, which may be retained by the legal department of the Receiving Party to confirm compliance with the non-use and non-disclosure provisions of this Agreement), and any Confidential Information of the Disclosing Party contained in its laboratory notebooks or databases, provided that each Receiving Party may retain and continue to use such Confidential Information of the Disclosing Party to the extent necessary to exercise any surviving rights, licenses or obligations under this Agreement. Notwithstanding the foregoing, a Receiving Party shall not be required to destroy any computer files created during automatic system back up that are subsequently stored securely by it and not readily accessible to its employees, consultants, or others who received the Disclosing Party’s Confidential Information under this Agreement.

9.9**Additional Effects of Termination by CAMP4 for Cause**. This Section 9.9 shall apply upon any termination of this Agreement in its entirety by CAMP4 under Section 9.2, Section 9.3, or Section 9.4:

9.9.1**License Grant**. Effective upon the effective date of termination of this Agreement, Fulcrum hereby grants to CAMP4 in the Field and in the Territory an exclusive, royalty-free, fully paid-up, license with the right to grant sublicenses, under any intellectual property rights Controlled by Fulcrum that are necessary or had been, prior to such termination, actually used by Fulcrum to exploit any Licensed Product, as such Licensed Product existed on the effective date of termination of this Agreement, to Research, Develop, Manufacture, use, Commercialize, or otherwise exploit such Licensed Products in the Field in the Territory.

9.9.2**Conveyance of Regulatory Filings**. Upon termination of this Agreement, Fulcrum will, to the extent not prohibited by Applicable Law, assign and transfer to CAMP4 or its designee, [***] any and all Regulatory Filings, including any Marketing Authorization obtained from Regulatory Authorities in the Territory, solely relating to a Licensed Product in the Field in the Territory. If Fulcrum is prohibited by Applicable Law from assigning or transferring Regulatory Filings to CAMP4 or its designee, then Fulcrum will promptly upon CAMP4's request (a) provide all such Regulatory Filings to CAMP4 or its designee and reasonably cooperate with CAMP4 and its designees to permit CAMP4 and its designees to make new Regulatory Filings for such Licensed Product in the Field in the Territory and (b) withdraw its own Regulatory Filings for the Licensed Product in the Territory.

9.10 **Additional Effects of Termination by Fulcrum for Convenience**. This Section 9.10shall apply upon any termination of this Agreement in its entirety by Fulcrum under Section 9.6:

9.10.1**Right to Negotiate**. On the written request of CAMP4 within [***] after the effective date of termination of this Agreement, Fulcrum will enter into good faith negotiations with CAMP4 for the grant to CAMP4 in the Field and in the Territory of an exclusive, royalty-bearing (or revenue sharing), license with the right to grant sublicenses, under any intellectual property rights Controlled by Fulcrum that are necessary or had been, prior to such termination, actually used by Fulcrum to exploit any Licensed Product, as such Licensed Product existed on the effective date of termination of this Agreement, to Research, Develop, Manufacture, use, Commercialize, or otherwise exploit such Licensed Products in the Field in the Territory.

9.10.2**Conveyance of Regulatory Filings**. Upon termination of this Agreement, Fulcrum will, to the extent not prohibited by Applicable Law, assign and transfer to CAMP4 or its designee, [***] any and all Regulatory Filings, including any Marketing Authorization obtained from Regulatory Authorities in the Territory, solely relating to a Licensed Product (other than Regulatory Filings relating to any Licensed Products Covered by a Valid Claim of a Patent owned by Fulcrum or its Affiliates or Sublicensees) in the Field in the Territory. If Fulcrum is prohibited by Applicable Law from assigning or transferring Regulatory Filings to CAMP4 or its designee, then Fulcrum will promptly upon CAMP4's request (a) provide all such Regulatory Filings to CAMP4 or its designee and reasonably cooperate with CAMP4 and its designees to permit CAMP4 and its designees to make new Regulatory Filings for such Licensed Product in the Field in the Territory and (b) withdraw its own Regulatory Filings for such Licensed Product in the Territory.

9.11**Survival**. Expiration or termination of this Agreement shall not relieve the Parties of any obligation or right accruing prior to such expiration or termination. Except as set forth below or elsewhere in this Agreement, the obligations and rights of the Parties under the following provisions of this Agreement shall survive expiration or termination of this Agreement: Article 1, Article 8, Sections 9.8-9.11, Article 10 and Article 11.

9.12**Bankruptcy Code**. If this Agreement is rejected by a Party as a debtor under Section 365 of the United States Bankruptcy Code or similar provision in the bankruptcy laws of another jurisdiction (the "***Code***"), then, notwithstanding anything else in this Agreement to the contrary, all licenses and rights to licenses granted under or pursuant to this Agreement by the Party in bankruptcy to the other Party are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the Code (or similar provision in the bankruptcy laws of the jurisdiction), licenses of rights to "intellectual property" as defined under Section 101(35A) of the Code (or similar provision in the bankruptcy laws of another applicable jurisdiction). The Parties agree that a Party that is a licensee of rights under this Agreement shall retain and may fully exercise all of its rights and elections under the Code, and that upon commencement of a bankruptcy proceeding by or against a Party under the Code, the other Party shall be entitled to a complete duplicate of, or complete access to (as such other Party deems appropriate), any such intellectual property and all embodiments of such intellectual property, if not already in such other Party's possession, shall be promptly delivered to such other Party: (a) upon any such commencement of a bankruptcy proceeding upon written request therefor by such other Party, unless the bankrupt Party elects to continue to perform all of its obligations under this Agreement; or (b) if not delivered under the foregoing subclause (a), upon the rejection of this Agreement by or on behalf of the bankrupt Party upon written request therefor by the other Party. The foregoing provisions of this Section 9.12 are without prejudice to any rights a Party may have arising under the Code.

ARTICLE 10

GOVERNING LAW; DISPUTE RESOLUTION

10.1**Governing Law**. This Agreement is governed by and will be construed in accordance with the laws of the State of Delaware, without reference to its conflict of laws principles. The United Nations Convention of International Contracts on the Sale of Goods (the Vienna Convention) does not apply to this Agreement.

10.2**Disputes**. The Parties recognize that controversies or claims arising out of, relating to, or in connection with this Agreement may arise from time to time. It is the objective of the Parties to establish procedures to facilitate the resolution of disputes in an expedient manner by mutual cooperation and without resort to litigation. To accomplish this objective, the Parties shall follow the procedures set forth in this Article 10 to resolve any dispute. If any dispute, claim or controversy of any nature arising out of or relating to this Agreement, including any action or claim based on tort, contract or statute, or concerning the interpretation, effect, termination, validity, performance or breach of this Agreement (each, a "***Dispute***"), arises between the Parties, either Party may refer the Dispute to Executive Officers of each Party for resolution within [***] of a written request by either Party to the other Party. Each Party, within [***] after a Party has received such written request from the other Party to so refer such Dispute, shall notify the other Party in writing of the Executive Officer to whom such Dispute is referred. If, after [***] the notice of Dispute, such Executive Officers have not succeeded in negotiating a resolution of the Dispute, either Party may seek to resolve the Dispute in any federal court having jurisdiction thereof located in Delaware as further described in Section 10.3.

10.3**Litigation; Equitable Relief**. The Federal courts located in Delaware shall have exclusive jurisdiction over, and shall be the exclusive venue for resolution of, any Dispute not resolved through the informal Dispute resolution procedures described above. Either Party may, at any time and without waiving any remedy under this Agreement, seek from any court having jurisdiction any temporary injunctive or provisional relief necessary to protect the rights or property of that Party. Any final judgment resolving a Dispute may be enforced by either Party in any court having appropriate jurisdiction.

ARTICLE 11

MISCELLANEOUS

11.1**Entire Agreement; Amendment**. This Agreement, including the Exhibits hereto, sets forth the complete, final and exclusive agreement and all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto with respect to the subject matter hereof and supersedes, as of the Effective Date, all prior and contemporaneous agreements and understandings between the Parties with respect to the subject matter, other than the Mutual Confidentiality Agreement. The foregoing may not be interpreted as a waiver of any remedies available to either Party as a result of any breach, prior to the Effective Date, by the other Party of its obligations under the Mutual Confidentiality Agreement. No subsequent alteration, amendment, change or addition to this Agreement shall be binding upon the Parties unless reduced to writing and signed by an authorized officer of each Party.

11.2**Limitation of Liability**. NEITHER PARTY MAY RECOVER FROM THE OTHER PARTY ANY SPECIAL, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES IN CONNECTION WITH THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH DAMAGES; *PROVIDED*, *HOWEVER*, THAT THIS SECTION 11.2 SHALL NOT BE CONSTRUED TO LIMIT (A) EITHER PARTY’S INDEMNIFICATION OBLIGATIONS UNDER Article 7 OR (B) DAMAGES AVAILABLE FOR A PARTY’S GROSS NEGLIGENCE, INTENTIONAL MISCONDUCT OR FRAUD OR FOR BREACH OF Article 8.

11.3**Independent Contractors**. The relationship between Fulcrum and CAMP4 created by this Agreement is solely that of independent contractors. This Agreement does not create any agency, distributorship, employee-employer, partnership, joint venture or similar business relationship between the Parties. Neither Party is a legal representative of the other Party, and neither Party can assume or create any obligation, representation, warranty, or guarantee, express or implied, on behalf of the other Party.

11.4**Notice**. Any notice required or permitted to be given by this Agreement must be in writing, in English. Any and all notices or other communications or deliveries required or permitted to be provided hereunder must be in writing and will be deemed given and effective if:
(a) delivered by hand or by overnight courier with tracking capabilities; (b) mailed postage prepaid by first class, registered, or certified mail; or (c) delivered by facsimile or electronic mail followed by delivery via either of the methods set forth in clauses (a) and (b) of this Section 11.4, in each case, addressed as set forth below unless changed by notice so given:

If to CAMP4: CAMP4 Therapeutics Corp.
Attn: CEO

One Kendall Square
Building 1400 West, 3rd Floor Cambridge, MA
02139
with a copy (which shall not constitute notice) to: Ropes & Gray LLP
Attn: Marc A. Rubenstein Prudential Tower
800 Boylston Street
Boston, MA 02199

If to Fulcrum: Fulcrum Therapeutics, Inc.
26 Landsdowne St
Cambridge, MA 02139 Attn:
General Counsel
with a copy (which shall not constitute notice) to: Goodwin Procter, LLP
Attn: Morag Peberdy 100
Cheapside
London, England EC2V 6DY

CAMP4 shall also provide a copy of any notice (via e-mail if available) to Fulcrum's Chief Legal Officer and to Fulcrum's Senior Vice President, Business and Corporate Development.

11.5**Severability**. If, for any reason, any part of this Agreement is adjudicated invalid, unenforceable, or illegal by a court of competent jurisdiction, such adjudication shall not, to the extent feasible, affect or impair, in whole or in part, the validity, enforceability, or legality of any remaining portions of this Agreement. All remaining portions will remain in full force and effect.

11.6**Non-Use of Names**. Neither Party will use the name, names, logos or trademarks of [CMCC, Harvard, DFCI or of their respective Affiliates, or HHMI, nor the name or photograph or other depiction of any employee or member of the staff of CMCC, Harvard, DFCI or their respective Affiliates or of HHMI [***] nor any adaptation of any of the foregoing, in any advertising, promotional, or sales literature without, in each case, prior written consent from CMCC, Harvard, DFCI or HHMI, as applicable, and from the individual staff member, employee, or student if such individual's name, photograph or depiction is used. Notwithstanding the above, a Party may state, including on its website, that it is licensed (or sub-licensed, as applicable) by CMCC, Harvard or DFCI under one or more patents or applications consistent with this Agreement, and a Party may comply with disclosure requirements of all Applicable Laws relating to its business, including United States and state securities laws. In addition, a Party may refer to publications by staff of BCH, Harvard or DFCI in the scientific literature. Neither Party shall use the name, trademark, logo, or physical likeness of the other Party, its Affiliates or their respective officers, directors or employees, or any adaptation of any of them, in any advertising, promotional or sales literature, without Fulcrum's prior written consent. In addition to the foregoing, neither Party shall, and shall ensure that its Affiliates and Sublicensees shall not, use or register the name

"Harvard" (alone or as part of another name) or any logos, seals, insignia or other words, names, symbols or devices that identify Harvard or any Harvard school, unit, division or affiliate ("Harvard Names") for any purpose except with the prior written approval of, and in accordance with restrictions required by, Harvard. Without limiting the foregoing, each Party shall, and shall ensure that its Affiliates and Sublicensees shall, cease all use of Harvard Names on the termination or expiration of this Agreement except as otherwise approved by Harvard. This restriction shall not apply to any information required by law to be disclosed to any governmental entity. Each Party shall require its Affiliates and Sublicensees to comply with the foregoing.

11.7**Assignment**. Except as provided in this Section 11.7, this Agreement may not be assigned or otherwise transferred, nor may any right or obligation hereunder be assigned or transferred, by either Party without the consent of the other Party; provided, however, that (and notwithstanding anything elsewhere in this Agreement to the contrary) either Party may, without such consent, assign this Agreement and its rights and obligations hereunder in whole: (a) to an Affiliate of such Party for such long as any such Affiliate remains an Affiliate; (b) in connection with the transfer or sale of all or substantially all of its assets or business related to the subject matter of this Agreement; or (c) pursuant to a merger or consolidation (or similar transaction) of the assigning Party. Any attempted assignment not in accordance with this Section 11.7 will be null, void, and of no legal effect. Any and all rights of Fulcrum hereunder may be exercised by one or more Affiliates of Fulcrum, without the need to sublicense, provided, however, that it is understood that all activities of such Affiliates are subject to the terms of this Agreement and that Fulcrum will remain obligated to CAMP4, and as applicable to HHMI, for the compliance by Fulcrum and its Affiliates with the terms of this Agreement.

11.8**Waivers**. The failure of a Party to insist upon strict performance of any provision of this Agreement or to exercise any right arising out of this Agreement shall neither impair that provision or right nor constitute a waiver of that provision or right, in whole or in part, in that instance or in any other instance. Any waiver by a Party of a particular provision or right shall be in writing, shall be as to a particular matter and, if applicable, for a particular period of time and shall be signed by such Party.

11.9**Force Majeure**. Each Party shall be excused from liability for the failure or delay in performance of any obligation under this Agreement by reason of any event beyond such Party's reasonable control, including, but not limited to, acts of God, fire, flood, explosion, earthquake, or other natural forces, war, civil unrest, terrorism, accident, destruction or other casualty, any lack or failure of transportation facilities, any lack or failure of supply of raw materials, any strike or labor disturbance, or any other event similar to those enumerated above. Such excuse from liability shall be effective only to the extent and duration of the event(s) causing the failure or delay in performance, provided that the Party has not caused such event(s) to occur. All delivery dates under this Agreement that have been affected by force majeure shall be tolled for the duration of such force majeure.

11.10**Interpretation**. The captions and headings to this Agreement are for convenience only, and are to be of no force or effect in construing or interpreting any of the provisions of this Agreement. Unless specified to the contrary, references to Articles, Sections, Schedules or Exhibits mean the particular Articles, Sections, Schedules or Exhibits to this Agreement and references to this Agreement include all Exhibits hereto. In the event of any conflict between the main body of this Agreement and any Exhibit hereto, the main body of this Agreement shall

prevail. Unless context otherwise clearly requires, whenever used in this Agreement: (a) the words “include” or “including” shall be construed as incorporating, also, “but not limited to” or “without limitation”; (b) the word “day” or “year” means a calendar day or year unless otherwise specified;
(c) the word “notice” means notice in writing (whether or not specifically stated) and shall include notices, consents, approvals and other written communications contemplated under this Agreement; (d) the words “shall” and “will” have interchangeable meanings for purposes of this Agreement; (e) words of any gender include the other gender; (f) references to any specific law, rule or regulation, or article, Section or other division thereof, shall be deemed to include the then- current amendments thereto or any replacement law, rule or regulation thereof; and (g) the term “or” will be interpreted in the inclusive sense commonly associated with the term “and/or” unless preceded by the word “either” or other language indicating the subjects of the conjunction are, or are intended to be, mutually exclusive.

11.11**Counterparts; Electronic Signatures**. This Agreement may be executed in any number of counterparts, each of which is deemed an original, but all of which together constitute one instrument. This Agreement may be executed and delivered electronically and upon such delivery such electronic signature will be deemed to have the same effect as if the original signature had been delivered to the other Party.

11.12**Expenses**. Each Party shall pay its own costs, charges and expenses incurred in connection with the negotiation, preparation and execution of this Agreement.

11.13**Further Assurances**. Fulcrum and CAMP4 hereby covenant and agree without the necessity of any further consideration, to execute, acknowledge and deliver any and all documents and take any action as may be reasonably necessary to carry out the intent and purposes of this Agreement.

11.14**Third Party Beneficiary Rights**. HHMI is not a party to this Agreement and has no liability under or due to this Agreement to Fulcrum, any Sublicensee, or any user of anything covered by this Agreement, but HHMI is an intended third-party beneficiary of this Agreement and certain of its provisions are for the benefit of HHMI and are enforceable by HHMI in its own name. Notwithstanding the foregoing, this Agreement is otherwise not intended to and shall not be construed to give any other Third Party any interest or rights (including any Third Party beneficiary rights) with respect to or in connection with any agreement or provision contained herein or contemplated hereby, except as otherwise provided for in this Agreement.

11.15**Cumulative Remedies**. No remedy referred to in this Agreement is intended to be exclusive unless explicitly stated to be so, but each shall be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under law.

In Witness Whereof, the Parties have caused this Agreement to be executed as of the Effective Date by their duly authorized representatives.

Fulcrum Therapeutics, Inc.

By: /s/ Robert J. Gould
Name: Robert J. Gould
Title: President & CEO

CAMP4 Therapeutics Corp.

By: /s/ Josh Mandel-Brehm
Name: Josh Mandel-Brehm
Title: President & CEO

<u>EXHIBIT A</u>

Licensed Patents

[***]

EXHIBIT B

CAMP4 Know-How and Materials

[***]

EXHIBIT C

Agreed form Press Release

Fulcrum Therapeutics Signs Exclusive Global License Agreement in Rare Hematology

— CAMP4 Therapeutics grants exclusive rights to advance novel therapies for Diamond-Blackfan Anemia —

CAMBRIDGE, Mass. – July 10, 2023 – **Fulcrum Therapeutics, Inc.®** (NASDAQ: FULC), a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined rare diseases, today announced that it has entered into a worldwide, exclusive license agreement with CAMP4 Therapeutics Corp., whereby Fulcrum will advance the discovery, development, and commercialization of novel therapeutic agents against an undisclosed target for the potential treatment of Diamond-Blackfan Anemia (DBA).

DBA is a congenital, rare blood disorder that affects an estimated 5,000 individuals worldwide. DBA is caused by genetic mutations in ribosomal subunits that halt red blood cell maturation and lead to anemia. Patients are usually diagnosed in infancy with the presentation of severe anemia and potential developmental abnormalities. Patients with DBA require lifelong management with corticosteroids and blood transfusions that are known for their toxicities and long-term complications.

"We are deeply committed to bringing hope and new options to patients suffering from rare hematologic diseases and are excited to expand on the work of CAMP4's pre-clinical DBA program," said Jeff Jacobs, Chief Scientific Officer, Fulcrum Therapeutics. "This agreement further strengthens our discovery pipeline and reinforces our strategy of addressing rare genetic conditions through small molecules."

Under the terms of the agreement, Fulcrum has been granted an exclusive, worldwide license to intellectual property arising from CAMP4's DBA program, including the right to research, develop, manufacture, and commercialize investigational compounds against an undisclosed target. In exchange, CAMP4 Therapeutics will receive an undisclosed upfront payment and up to $70 million in additional payments, upon the achievement of certain development, regulatory, and commercial milestones. Fulcrum will assume sole responsibility for research, development, manufacturing and commercialization costs and activities, and will pay tiered royalties on future commercial sales.

"Our mission is to harness the power of the cell's transcriptional regulators to unlock new options for people living with genetic diseases like DBA," said Josh Mandel-Brehm, Chief Executive Officer, CAMP4 Therapeutics. "By uniting our scientific insights with Fulcrum's deep expertise in hematology and small molecule development, this agreement will help accelerate the discovery and delivery of ground-breaking therapies for this underserved community."

About Fulcrum Therapeutics

Fulcrum Therapeutics is a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined rare diseases in areas of high unmet medical need. Fulcrum's two lead programs in clinical development are losmapimod, a small molecule for the treatment of facioscapulohumeral muscular dystrophy (FSHD), and FTX-6058, a small molecule designed to increase expression of fetal hemoglobin for the treatment of sickle cell disease (SCD) and other hemoglobinopathies, which is currently under a full clinical hold issued by the U.S. Food and Drug Administration. The company's proprietary product engine, FulcrumSeek™, identifies drug targets that can modulate gene expression to treat the known root cause or consequences of gene mis-expression. For more information, visit **www.fulcrumtx.com**.

Forward-Looking Statements

This press release contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this press release are forward-looking statements, including express or implied statements regarding Fulcrum’s exclusive license agreement with CAMP4 Therapeutics, and the milestone and royalty payments thereunder; Fulcrum’s ability to develop a therapy for DBA; and the potential effect of this agreement on Fulcrum’s discovery pipeline; among others. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, risks associated with biopharmaceutical development, Fulcrum’s ability to continue to advance its product candidates into and through clinical trials; initiate and enroll clinical trials on the timeline expected or at all; obtain and maintain necessary approvals from the FDA and other regulatory authorities; replicate in clinical trials positive results found in preclinical studies and/or earlier-stage clinical trials; obtain, maintain or protect intellectual property rights related to its product candidates; manage expenses; realize the anticipated benefits of the strategic realignment; manage executive and employee turnover; and raise the substantial additional capital needed to achieve its business objectives, among others. For a discussion of other risks and uncertainties, and other important factors, any of which could cause Fulcrum’s actual results to differ from those contained in the forward-looking statements, see the “Risk Factors” section, as well as discussions of potential risks, uncertainties, and other important factors, in Fulcrum’s most recent filings with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent Fulcrum’s views as of the date hereof and should not be relied upon as representing Fulcrum’s views as of any date subsequent to the date hereof. Fulcrum anticipates that subsequent events and developments will cause Fulcrum’s views to change. However, while Fulcrum may elect to update these forward-looking statements at some point in the future, Fulcrum specifically disclaims any obligation to do so.

Contact Information:

Investors:
Chris Calabrese LifeSci
Advisors, LLC
ccalabrese@lifesciadvisors.com 917-
680-5608

Media:
Dee Smith
Executive Director, Corporate Communications Fulcrum
Therapeutics, Inc.
dsmith@fulcrumtx.com
202-746-1324

EXHIBIT D

Development Plan

[***]

FULCRUM THERAPEUTICS, INC.
EXECUTIVEEMPLOYMENT AGREEMENT

THIS EXECUTIVE EMPLOYMENT AGREEMENT (the "Agreement") is made as of August 7, 2023 (the "Effective Date") by and between Fulcrum Therapeutics, Inc. (the "Company") and Alan Musso (the "Executive") (the Company and the Executive each a "Party" and together the "Parties").

RECITALS

WHEREAS, the Company desires to employ the Executive as its Chief Financial Officer; and

WHEREAS, the Executive has agreed to accept such employment on the terms and conditions set forth in this Agreement.

NOW, THEREFORE, in consideration of the foregoing and of the respective covenants and agreements of the Parties herein contained, the Parties hereto agree as follows:

1.*Start Date; Term of Employment*. The Executive's employment under this Agreement will commence on August 7, 2023 (the "Start Date") and will continue until terminated by either Party. The effective date of any termination of the Executive's employment hereunder is hereinafter referred to as the "Termination Date", and the period of time between the Start Date and the Termination Date is hereinafter referred to as the "Term of Employment". Effective upon any Termination Date, this Agreement will automatically terminate and will be of no further force or effect, except as otherwise provided in Section 14 hereof, and the Executive shall immediately resign, in writing, from all positions then held by the Executive with the Company and its affiliates, unless otherwise expressly agreed to by the Company and the Executive. For the avoidance of doubt, the Executive's employment is at-will, and either the Executive or the Company may terminate the Executive's employment hereunder any time, for any or no reason, without advance notice (except for any notice expressly required under Section 6 below).

2.*Position; Location.* During the Term of Employment, the Executive shall serve as the Chief Financial Officer of the Company (the "Position"). Executive will spend on average at least 40% of his work time either in the Company's office in Cambridge, Massachusetts, or in business travel as reasonably required by the Executive's job duties, and shall otherwise work remotely from Executive's home office in Executive's principal state of residence in the State of North Carolina, or such other state; provided that Executive agrees not to relocate outside of the State of North Carolina without prior written notice to the President and Chief Executive Officer.

3.*Duties*. During the Term of Employment, the Executive shall be responsible for the performance of those duties, and shall have such authorities and responsibilities, as are consistent with the Executive's Position, and such other duties, authorities and responsibilities not inconsistent with the Executive's Position as may be assigned to the Executive by the President and Chief Executive Officer from time to time. The Executive shall report to President and Chief Executive Officer of the Company and shall perform and discharge faithfully, diligently, and to the best of the Executive's ability, the Executive's duties and responsibilities hereunder. The Executive shall devote his full working time and efforts to the business and affairs of the

Company and its affiliates. Notwithstanding the foregoing, the Executive may serve on other boards of directors, with the approval of the Board of Directors of the Company (the "Board") which will not be unreasonably withheld, or engage in religious, charitable or other activities as long as such services and activities are approved by the Board and do not materially interfere with the Executive's performance of his duties to the Company as provided in this Agreement. The Executive agrees to abide by the rules, regulations, instructions, personnel practices and policies of the Company and any changes therein that may be adopted from time to time by the Company.

4.*Compensation*. As full compensation for all services rendered by the Executive to the Company and any affiliate thereof, during the Term of Employment, the Company will provide to the Executive the following:

(a)*Base Salary*. Effective as of the Start Date, the Executive shall receive a base salary at the annualized rate of $450,000, less all applicable withholdings and deductions (the "Base Salary"). The Executive's Base Salary shall be paid in equal installments in accordance with the Company's regularly established payroll procedures. The Executive's Base Salary will be reviewed on an annual or more frequent basis by the Board and is subject to change in the sole and absolute discretion of the Board.

(b)*Annual Discretionary Bonus*. For each calendar year during the Term of Employment (prorated for the Executive's first calendar year of employment), the Executive will be eligible to earn an annual discretionary performance bonus (the "Annual Discretionary Bonus") in an initial amount of up to 40% of the Executive's Base Salary (the "Target Bonus"), based upon the Board's assessment of the Executive's performance and the Company's attainment of targeted goals as set by the Board in its sole and absolute discretion. To the extent the Executive's Base Salary and/or target bonus percentage of Base Salary is changed during the year to which the performance bonus relates, the Target Bonus shall be calculated based on Base Salary actually paid during such year (and not solely on the Executive's Base Salary at the end of such year) and applying the initial target bonus percentage of Base Salary and the revised target bonus percentage of Base Salary based on the portion of the year during which each was in effect. The Board may determine to pay any earned Annual Discretionary Bonus in the form of cash, vested equity award(s), or a combination of cash and equity, in its sole and absolute discretion. Following the close of each calendar year, the Board will determine whether the Executive has achieved an Annual Discretionary Bonus for such year, and the amount of any such Annual Discretionary Bonus, based on the set criteria (which, for the avoidance of doubt, may be less than the Target Bonus). The Annual Discretionary Bonus, if earned, will be paid by no later than March 15 of the calendar year after the year to which it relates. No amount of the Annual Discretionary Bonus is guaranteed, and the Executive must remain employed by the Company in good standing through the date of payment of an Annual Discretionary Bonus in order to earn and receive such bonus, except as may be specifically set forth in Section 7 below. The Executive's bonus eligibility, and the terms and conditions of the bonus (including the Target Bonus amount), will be reviewed on an annual or more frequent basis by the Board and are subject to change in the discretion of the Board.

(c)*Initial Stock Option Award*. On the Start Date, the Company will grant to the Executive, subject to the Executive's continued employment with the Company through the grant date, a one- time award consisting of nonqualified options to purchase 432,800 shares of the

Company's common stock (the "Shares") at a per-Share exercise price equal to the grant date fair market value of one Share (the "Initial Option Award"), subject to all of the terms and conditions of the Company's incentive equity plan and/or inducement plan, as applicable, an individual award agreement, and any ancillary agreements with the Company that the Executive may be required to enter into as a condition of such grant (collectively, the "Equity Documents"), which will provide, among other things, that the Initial Option Award will vest and become exercisable over 4 years as follows: (i) as to 25% of the Shares underlying the Initial Option Award on the first anniversary of the Start Date and (ii) as to an additional 6.25% of the Shares underlying the Initial Option Award on the last day of each of the next 12 successive calendar quarters, provided in each case that the Executive remains employed by the Company and in compliance with the Equity Documents through each such vesting date. In the event of any conflict between any terms of this Agreement and any terms of the Equity Documents, the terms of the Equity Documents will prevail.

(d)*Performance Based Equity Award*. The Executive will be eligible to receive an additional 61,822 shares which shall be subject to performance objectives and if achieved, this grant shall fully vest six months after the Employment Start Date. Failure to achieve all performance objectives within six months of the Employment Start Date shall mean that the Performance Based Equity Award shall be forfeited in its entirety.

(e)*Additional Discretionary Equity Awards*. During the Term of Employment, the Executive will be eligible to receive additional incentive equity awards, if any, at such times and on such terms and conditions as the Board shall, in its sole discretion, determine.

(f)*Paid Time Off*. During the Term of Employment, the Executive shall be entitled to paid time off, vacation time plus sick time, consistent with the Company's policies.

(g)*Business Expenses*. Upon presentation of such substantiation and documentation as the Company may specify from time to time, the Executive will be reimbursed in accordance with the Company's expense reimbursement policy as in effect from time to time for all eligible out-of- pocket business expenses incurred and paid by the Executive during the Term of Employment.

(h)*Employee Benefits*. During the Term of Employment, the Executive will be eligible to participate in any employee benefit plan maintained by the Company for the benefit of its employees generally, subject to all of the terms and conditions (including eligibility requirements) of such plan. Notwithstanding the foregoing, the Company may modify or terminate any employee benefit plan at any time, in its sole and absolute discretion.

(i)*Housing and Travel Allowance*. The Company will provide the Executive with an additional cash allowance of up to $75,000 annually (pro-rated for any partial calendar year) to be applied by the Executive solely towards the rental cost of a personal apartment in the Greater Boston metropolitan region and to transportation expenses for Executive's regular commuting trips to the Company's offices in Cambridge, Massachusetts, in each case solely to the extent such costs or expenses are incurred during the Term of Employment (the "Housing and Travel Allowance"), which will be paid to the Executive on a monthly basis in arrears, subject to presentation by the Executive of such substantiation and documentation as the Company may specify from time to time. To the extent that such Housing and Travel Allowance will constitute taxable income to the Executive for a given calendar year, the Company will also provide the Executive with an additional cash gross-up amount (the "Housing Gross-Up Payment") equal to the estimated amount of such taxable income (estimated at the highest federal and state tax rates applicable to a person living in the Commonwealth of Massachusetts), which will be paid to the Executive on or before December 31 of such year, regardless of whether Executive is employed through such payment date (but provided that Executive was employed by the Company for at least one day during such year). Annually the President and Chief Executive Officer will review and determine in its sole discretion after good faith consultation with the Executive appropriate adjustments, if any, to the amount of the Housing and Travel Allowance for each subsequent year.

5.*Restrictive Covenants Agreement*. The Executive hereby acknowledges that in connection with entering into this Agreement, the Executive shall be required to enter into, and agrees to strictly abide by, an Employee Confidentiality and Assignment Agreement with the Company in the form attached as Exhibit A hereto (the "ECAA").

6.*Employment Termination*. This Agreement, the Term of Employment, and the employment of the Executive shall terminate upon the occurrence of any of the following:

(a)Automatically and immediately upon the death or "Disability" of the Executive. As used in this Agreement, the term "Disability" shall mean a physical or mental illness or disability that prevents the Executive from performing the duties of the Executive's position for a period of more than any three consecutive months or for periods aggregating more than twenty-six weeks. The Company shall determine in good faith and in its sole discretion whether the Executive is unable to perform the services provided for herein. The Executive will cooperate in all respects with the Company if a question arises as to whether the Executive has become Disabled (including, without limitation, submitting to reasonable examinations by one or more medical doctors and other health care specialists selected by the Company).

(b)At the election of the Company, with or without "Cause" (as defined below), immediately upon written notice by the Company to the Executive. As used in this Agreement, "Cause" shall mean:

(i) Executive's dishonest statements or acts with respect to the Company or any affiliate of the Company (each, a "Group Company"), or any current or prospective customers, suppliers, vendors or other third parties with which such entity does business that results in or, in the good faith judgement of the Board, is anticipated to result in, material harm to any Group Company;

(ii) Executive's conviction of (including any plea of guilty or nolo contendere to), or indictment for, (A) a felony or (B) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud, or that materially and permanently impairs the Executive's ability to perform the Executive's duties with any Group Company;

(iii) Executive's gross negligence, willful misconduct or insubordination with respect to any Group Company that results in or, in the good faith judgement of the Board, is anticipated to result in, material harm to any Group Company, provided, however, that the Executive shall have a period of not less than ten (10) days to cure any curable act or omission (as determined by the Board in its good faith discretion) constituting Cause described in this Section 6(b)(iii) following the Board's delivery to the Executive of written notice of such act or omission;

(iv) Executive's theft, fraud, embezzlement, breach of fiduciary duty or material falsification of any documents or records of any Group Company;

(v) Executive's material failure to abide by any Group Company's code of conduct or other policies (including policies relating to confidentiality and workplace conduct);

(vi) Executive's willful failure to perform the Executive's duties hereunder after written notice from the Board of such failure;

(vii) Executive's unauthorized use, misappropriation, destruction or diversion of any tangible or intangible asset or corporate opportunity of a Group Company (including the Executive's improper use or disclosure of a Group Company's confidential or proprietary information);

(viii) Executive's willful failure to cooperate with the Company and its legal counsel in connection with any investigation or other legal or similar proceeding involving any Group Company; or

(ix) Executive's material violation of this Agreement or of any provision of any other agreement(s) between the Executive and the Company (including, without limitation, any provision relating to nonsolicitation, nondisclosure and/or assignment of inventions).

(c) At the election of the Executive, with or without "Good Reason" (as defined below), immediately upon written notice by the Executive to the Company (subject, if it is with Good Reason, to the timing provisions set forth in the definition of Good Reason). As used in this Agreement, "Good Reason" shall mean, without the Executive's consent:

(i) a material diminution of the Executive's Base Salary, other than in connection with, and substantially proportionate to, reductions by the Company of the base compensation of all or substantially all senior executives of the Company;

(ii) a material diminution in the Executive's duties, authority or responsibilities (other than temporarily while physically or mentally incapacitated or as required by applicable law);

(iii) the Company's requiring Executive to relocate Executive's primary office more than fifty (50) miles from the Executive's then-current primary office, which increases the Executive's one-way commute distance; or

(iv) any material breach of this Agreement between the Company and the Executive by the Company not otherwise covered by this paragraph;

provided, however, that in each case, the Company shall have a period of not less than thirty (30) days to cure any act constituting Good Reason following Executive's delivery to the Company of written notice within sixty (60) days of the action or omission constituting Good Reason, and that the Executive actually terminates employment within thirty (30) days following the expiration of the Company's cure period.

7. *Effect of Termination*.

(a)*All Terminations Other Than by the Company Without Cause or by the Executive With Good Reason*. If the Executive's employment is terminated under any circumstances other than a Qualifying Termination (as defined below) (including a voluntary termination by the Executive without Good Reason pursuant to Section 6(c), a termination by the Company for Cause pursuant to Section 6(b) or due to the Executive's death or Disability pursuant to Section 6(a)), the Company's obligations under this Agreement shall immediately cease and the Executive shall only be entitled to receive (i) the Base Salary that has accrued and to which the Executive is entitled as of the Termination Date and to the extent consistent with general Company policy, to be paid in accordance with the Company's established payroll procedure and applicable law but no later than the next regularly scheduled pay period, (ii) unreimbursed business expenses for which expenses the Executive has timely submitted appropriate documentation in accordance with Section 4(f) hereof, to be paid in accordance with the Company's expense reimbursement policy, and (iii) any amounts or benefits to which the Executive is then entitled under the terms of the benefit plans then-sponsored by the Company in accordance with their terms (and not accelerated to the extent acceleration does not satisfy Section 409A of the Internal Revenue Code of 1986, as amended (the "<u>Code</u>")) (the payments described in this sentence, the "<u>Accrued Obligations</u>").

(b)*Termination by the Company Without Cause or by the Executive With Good Reason Prior to or More Than Twelve Months Following a Change in Control and Subject to Executive's Good Performance for at Least Twelve Months.* If the Executive's employment is terminated by the Company without Cause pursuant to Section 6(b) (which, for the avoidance of doubt, does not include any termination due to the Executive's death or Disability pursuant to Section 6(a)) or by the Executive with Good Reason pursuant to Section 6(c) (in either case, a "<u>Qualifying Termination</u>") prior to or more than twelve (12) months following a Change in Control (as defined below), and such Qualifying Termination occurs after the Executive has completed at least twelve
(12) months of employment with good performance for the Company (as determined by the Board in its sole and absolute discretion), then the Executive shall be entitled to the Accrued Obligations. In addition, and subject to Section 8 and the conditions of Section 7(d), in the case of a termination described in the preceding sentence, the Company shall: [(i) continue to pay to the Executive, in equal periodic installments in accordance with the Company's regularly established payroll procedures (not less frequently than monthly), the Executive's Base Salary for a period of nine (9) months commencing on the Payment Date (as defined below); (ii) pay to the Executive, in a single lump sum on the Payment Date, an amount equal to 100% of the Executive's Target Bonus for the year in which termination occurs; and (iii) provided the Executive is eligible for and timely elects to continue receiving group medical coverage pursuant to the "COBRA" law, continue to pay (but in no event longer than nine (9) months following the Executive's Termination Date) the share of

the premium for such coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage, unless the Company's provision of such COBRA subsidy will violate the nondiscrimination requirements of applicable law, in which case this benefit will not apply] (collectively, the "Severance Benefits").

(c)*Termination by the Company Without Cause or by the Executive With Good Reason Within Twelve Months Following a Change in Control.* If a Qualifying Termination occurs within twelve (12) months following a Change in Control, then the Executive shall be entitled to the Accrued Obligations. In addition, and subject to Section 8 and the conditions of Section 7(d), the Company shall: [(i) continue to pay to the Executive, in equal periodic installments in accordance with the Company's regularly established payroll procedures (not less frequently than monthly), the Executive's Base Salary (or, if higher, the Executive's Base Salary in effect immediately prior to the Change in Control) for a period of twelve (12) months commencing on the Payment Date;
(ii) pay to the Executive, in a single lump sum on the Payment Date, an amount equal to 100% of the Executive's Target Bonus for the year in which termination occurs or, if higher, the Executive's Target Bonus immediately prior to the Change in Control; (iii) provided the Executive is eligible for and timely elects to continue receiving group medical coverage pursuant to the "COBRA" law, continue to pay (but in no event longer than twelve (12) months following the Executive's Termination Date) the share of the premium for such coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage, unless the Company's provision of such COBRA subsidy will violate the nondiscrimination requirements of applicable law, in which case this benefit will not apply; and (iv) provide that the vesting of the Executive's then-unvested equity awards that vest based solely on the passage of time shall be accelerated, such that all then-unvested equity awards that vest based solely on the passage of time vest and become fully exercisable or non-forfeitable as of the Termination Date] (collectively, the "Change in Control Severance Benefits").

(d)*Release*. As a condition of the Executive's receipt of the Severance Benefits or the Change in Control Severance Benefits, as applicable, the Executive must execute and deliver to the Company a severance and release of claims agreement in a form to be provided by the Company (the "Severance Agreement"), which Severance Agreement must become irrevocable within 60 days following the Executive's Termination Date (or such shorter period as may be directed by the Company). The Severance Benefits or the Change in Control Severance Benefits (other than any COBRA subsidy), as applicable, will be paid or commence to be paid in the first regular payroll beginning after the Severance Agreement becomes effective and irrevocable, provided that if the foregoing 60 day period (or such shorter period as may be directed by the Company) would end in a calendar year subsequent to the year in which the Executive's employment ends, the Severance Benefits or Change in Control Severance Benefits (other than any COBRA subsidy), as applicable, will not be paid or begin to be paid before the first payroll of the subsequent calendar year (the date the Severance Benefits or Change in Control Severance Benefits, as applicable, commence pursuant to this sentence, the "Payment Date"). The Executive must continue to comply with the ECAA and any similar agreement with the Company or its affiliates in order to be eligible to continue receiving the Severance Benefits or Change in Control Severance Benefits, as applicable.

(e)*Change in Control Definition*. For purposes of this Agreement, "Change in Control" shall mean the occurrence of any of the following events, *provided that such event or occurrence* *constitutes a change in the ownership or effective control of the Company, or a change in the ownership of a substantial portion of the assets of the Company, as defined in Treasury Regulation §§ 1.409A-3(i)(5)(v), (vi) and (vii)*: (i) the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934 (the "Exchange Act")) (a "Person") of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 under the Exchange Act) fifty percent (50%) or more of either (x) the then-outstanding shares of common stock of the Company (the "Outstanding Company Common Stock") or (y) the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the "Outstanding Company Voting Securities"); provided, however, that for purposes of this subsection (i), the following acquisitions shall not constitute a Change in Control: (1) any acquisition directly from the Company or (2) any acquisition by any entity pursuant to a Business Combination (as defined below) which complies with clauses (x) and (y) of subsection (iii) of this definition; or (ii) a change in the composition of the Board that results in the Continuing Directors (as defined below) no longer constituting a majority of the Board (or, if applicable, the Board of Directors of a successor corporation to the Company), where the term "Continuing Director" means at any date a member of the Board (x) who was a member of the Board on the Effective Date or (y) who was nominated or elected subsequent to such date by at least a majority of the directors who were Continuing Directors at the time of such nomination or election or whose election to the Board was recommended or endorsed by at least a majority of the directors who were Continuing Directors at the time of such nomination or election; provided, however, that there shall be excluded from this clause (y) any individual whose initial assumption of office occurred as a result of an actual or threatened election contest with respect to the election or removal of directors or other actual or threatened solicitation of proxies or consents, by or on behalf of a person other than the Board; or (iii) the consummation of a merger, consolidation, reorganization, recapitalization or share exchange involving the Company, or a sale or other disposition of all or substantially all of the assets of the Company (a "Business Combination"), unless, immediately following such Business Combination, each of the following two (2) conditions is satisfied: (x) all or substantially all of the individuals and entities who were the beneficial owners of the Outstanding Company Common Stock and Outstanding Company Voting Securities immediately prior to such Business Combination beneficially own, directly or indirectly, more than fifty percent (50%) of the then-outstanding shares of common stock and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors, respectively, of the resulting or acquiring corporation in such Business Combination (which shall include, without limitation, a corporation which as a result of such transaction owns the Company or substantially all of the Company's assets either directly or through one (1) or more subsidiaries) (such resulting or acquiring corporation is referred to herein as the "Acquiring Corporation") in substantially the same proportions as their ownership of the Outstanding Company Common Stock and Outstanding Company Voting Securities, respectively, immediately prior to such Business Combination and (y) no Person (excluding any employee benefit plan (or related trust) maintained or sponsored by the Company or by the Acquiring Corporation) beneficially owns, directly or indirectly, fifty percent (50%) or more of the then-outstanding shares of common stock of the Acquiring Corporation, or of the combined voting power of the then- outstanding securities of such corporation entitled to vote generally in the election of directors (except to the extent that such ownership existed prior to the Business Combination); or (iv) the liquidation or dissolution of the Company.

8. *Tax Matters.*

(a)*Withholding*. The Company may withhold from any compensation and benefits payable under this Agreement all applicable federal, state, local, or other taxes, and any other applicable withholdings and deductions.

(b) *Section 409A.*

(i) Although the Company does not guarantee the tax treatment of any payments or benefits under this Agreement, the intent of the Parties is that the payments and benefits under this Agreement be exempt from or, to the extent not exempt, comply with, Section 409A of the Code and the regulations and guidance promulgated thereunder (collectively "Section 409A"), and, accordingly, to the maximum extent possible, this Agreement will be interpreted and construed consistent with such intent. Notwithstanding the foregoing, the Company does not guarantee any particular tax result, and in no event whatsoever will the Company, its affiliates, or their respective officers, directors, employees, counsel or other service providers, be liable for any tax, interest or penalty that may be imposed on the Executive by Section 409A or damages for failing to comply with Section 409A.

(ii) For purposes of Section 409A, the Executive's right to receive installment payments pursuant to this Agreement shall be treated as a right to receive a series of separate payments and, accordingly, each installment payment will at all times be considered a separate and distinct payment. Whenever a payment hereunder specifies a payment period with reference to a number of days, the actual date of payment within the specified period shall be within the sole discretion of the Company.

(iii) To the extent that reimbursements or other in-kind benefits hereunder constitute "deferred compensation" subject to Section 409A, (x) all expenses or other reimbursements hereunder will be made on or prior to the last day of the taxable year following the taxable year in which such expenses were incurred by the Executive, (y) any right to reimbursement or in-kind benefits will not be subject to liquidation or exchange for another benefit, and (z) no such reimbursement, expenses eligible for reimbursement, or in-kind benefits provided in any taxable year will in any way affect the expenses eligible for reimbursement, or in-kind benefits to be provided, in any other taxable year.

(iv) Any other provision of this Agreement to the contrary notwithstanding, in no event will any payment or benefit hereunder that constitutes "deferred compensation" subject to Section 409A be subject to offset by any other amount unless otherwise permitted by Section 409A.

(v) A termination of employment will not be deemed to have occurred for purposes of any provision of this Agreement providing for the payment of any amounts or benefits that constitute "deferred compensation" subject to Section 409A upon or following a termination of employment, unless such termination is also a "separation from service" within the meaning of Section 409A, and, for purposes of any such provision, all references in this Agreement to the Executive's "termination", "termination of employment" or like terms will mean the Executive's "separation from service" with the Company, and the date of such separation from service will be the date of termination for purposes of any such payment or benefit.

(vi) Notwithstanding any other provision of this Agreement to the contrary, if, at the time of the Executive's separation from service, the Executive is a "specified employee" within the meaning and in accordance with Treasury Regulation Section 1.409A-1(i), then the Company will defer the payment or commencement of any "deferred compensation" subject to Section 409A that is payable upon separation from service (without any reduction in such payments or benefits ultimately paid or provided to the Executive) until the date that is six (6) months following separation from service or, if earlier, the earliest other date as is permitted under Section 409A (and any amounts that otherwise would have been paid during this deferral period will be paid in a lump sum on the day after the expiration of the six
(6) month period or such shorter period, if applicable). The Company will determine in its sole discretion all matters relating to who is a "specified employee" and the application of and effects of the change in such determination.

(c)*Section 280G*. In the event that any payments and other benefits provided for in this Agreement or otherwise payable to the Executive constitute "parachute payments" within the meaning of Section 280G of the Code, and, but for this paragraph, would be subject to the excise tax imposed by Section 4999 of the Code, then any post-termination severance payments and benefits payable under this Agreement or otherwise will be either (1) delivered in full or (2) delivered as to such lesser extent which would result in no portion of such payments and benefits being subject to excise tax under Section 4999 of the Code, whichever of the foregoing amounts, taking into account the applicable federal, state and local income taxes and the excise tax imposed by Section 4999 of the Code, results in the receipt by the Executive, on an after-tax basis, of the greatest amount of payments and benefits, notwithstanding that all or some portion of such benefits may be taxable under Section 4999 of the Code. If a reduction in the Executive's payments and benefits is necessitated by the preceding sentence, such reduction will occur in the following order:
(i) any cash amounts payable to the Executive, (ii) any benefits valued as parachute payments, and
(iii) acceleration of vesting of any equity awards. Any determination required under this paragraph will be made in writing by the Company's independent public accountants (the "Firm"), whose determination will be conclusive and binding upon the Executive and the Company. For purposes of making the calculations required by this paragraph, the Firm may make reasonable assumptions and approximations concerning applicable taxes and may rely on reasonable, good faith interpretations concerning the application of Sections 280G and 4999 of the Code. The Company and the Executive will furnish to the Firm such information and documents as the Firm may reasonably request in order to make a determination under this paragraph. The Company will bear all costs the Firm may incur in connection with any calculations contemplated by this paragraph.

9.*Clawback*. To the maximum extent permitted by applicable law, all amounts paid or provided to the Executive hereunder shall be subject to any clawback or recoupment policy that may be maintained by the Company from time to time, and the requirements of any law or regulation applicable to the Company and governing the clawback or recoupment of executive compensation, or as set forth in any final non-appealable order by any court of competent jurisdiction or arbitrator.

10.*Absence of Restrictions*. The Executive represents and warrants that the Executive is not bound by any employment contracts, restrictive covenants or other restrictions that prevent the Executive from entering into employment with, or carrying out the Executive's responsibilities for, the Company, or which are in any way inconsistent with any of the terms of this Agreement.

11.*Notice*. Any notice delivered under this Agreement shall be deemed duly delivered three (3) business days after it is sent by registered or certified mail, return receipt requested, postage prepaid, one (1) business day after it is sent for next-business day delivery via a reputable nationwide overnight courier service, or immediately upon hand delivery, in each case to the address of the recipient set forth below.

To Executive:

At the address set forth in the Executive's personnel file To Company:
Fulcrum Therapeutics, Inc.
26 Landsdowne Street, 5th Floor Cambridge, MA 02139

Either Party may change the address to which notices are to be delivered by giving notice of such change to the other Party in the manner set forth in this Section 11.

12.*Applicable Law; Jury Trial Waiver*. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts (without reference to the conflict of laws provisions thereof). Any action, suit or other legal proceeding arising under or relating to any provision of this Agreement shall be commenced only in a court of the Commonwealth of Massachusetts (or, if appropriate, a federal court located within the Commonwealth of Massachusetts), and the Company and the Executive each consents to the jurisdiction of such a court. The Company and the Executive each hereby irrevocably waives any right to a trial by jury in any action, suit or other legal proceeding arising under or relating to any provision of this Agreement.

13.*Successors and Assigns*. This Agreement shall be binding upon and inure to the benefit of both Parties and their respective successors and assigns, including any corporation with which or into which the Company may be merged or which may succeed to its assets or business (and, as used in this Agreement, "<u>Company</u>" will mean the Company and any such successor corporation); provided, however, that the obligations of the Executive are personal and shall not be assigned by the Executive.

14.*Survival*. Sections 5 and 7 through 22 hereof will survive and continue in full force and effect in accordance with their respective terms notwithstanding any expiration or termination of the Term of Employment and/or this Agreement.

15.*Pre-Employment Checks*. The Executive acknowledges and agrees that the Executive's employment, and this Agreement, are contingent upon satisfactory completion prior to the Start Date of pre-employment screening activities, including favorable reference checks of former employment, verification of the Executive's ability to work in the United States, and educational background and criminal history checks. The Executive agrees to assist the Company as needed to facilitate the timely completion of such checks.

16.*Acknowledgment*. The Executive states and represents that the Executive has had an opportunity to fully discuss and review the terms of this Agreement with an attorney. The Executive further states and represents that the Executive has carefully read this Agreement, understands the contents herein, freely and voluntarily assents to all of the terms and conditions hereof, and signs the Executive's name of the Executive's own free act.

17.*No Oral Modification, Waiver, Cancellation or Discharge*. This Agreement may be amended or modified only by a written instrument executed by both the Company and the Executive. No delay or omission by the Company in exercising any right under this Agreement shall operate as a waiver of that or any other right. A waiver or consent given by the Company on any one occasion shall be effective only in that instance and shall not be construed as a bar to or waiver of any right on any other occasion.

18.*Captions and Pronouns*. The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit or affect the scope or substance of any section of this Agreement. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular forms of nouns and pronouns shall include the plural, and vice versa.

19.*Interpretation*. The Parties agree that this Agreement will be construed without regard to any presumption or rule requiring construction or interpretation against the drafting Party. References in this Agreement to "include" or "including" should be read as though they said "without limitation" or equivalent forms. References in this Agreement to the "Board" shall include any authorized committee thereof.

20.*Severability*. Each provision of this Agreement must be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be prohibited by or invalid under applicable law, such provision will be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of such provision or the remaining provisions of this Agreement. Moreover, if a court of competent jurisdiction determines any of the provisions contained in this Agreement to be unenforceable because the provision is excessively broad in scope, whether as to duration, activity, geographic application, subject or otherwise, it will be construed, by limiting or reducing it to the extent legally permitted, so as to be enforceable to the extent compatible with then applicable law to achieve the intent of the Parties.

21.*Counterparts*. This Agreement may be executed in several counterparts, each of which will be deemed to be an original but all of which together will constitute one and the same instrument. Facsimile, PDF, and electronic counterpart signatures to and versions of this Agreement will be acceptable and binding on the Parties.

22.*Entire Agreement*. This Agreement, including the agreements and arrangements referenced herein, constitutes the entire agreement between the Parties and supersedes all prior agreements and understandings, whether written or oral, relating to the subject matter of this Agreement.

[Signatures on Page Following]

IN WITNESS WHEREOF, the Parties hereto have executed this Agreement as of the day and year set forth above.

FULCRUM THERAPEUTICS, INC.

By:	/s/ Kim Hazen
Name:	Kim Hazen
Title:	Chief People Officer

EXECUTIVE:

By:	/s/ Alan Musso
Name:	Alan Musso

Exhibit 31.1

CERTIFICATION 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, Alex C. Sapir, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Fulcrum 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 7, 2023	By:	/s/ Alex C. Sapir
		Alex C. Sapir
		President and Chief Executive Officer
		(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION 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, Alan Musso, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Fulcrum 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 7, 2023	By:	/s/ Alan Musso
		Alan Musso
		Chief Financial Officer
		(Principal Financial Officer)

Exhibit 32.1

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Quarterly Report on Form 10-Q of Fulcrum Therapeutics, Inc. (the “Company”) for the period ended September 30, 2023, as filed with the Securities and Exchange Commission on the date hereof (the “Report”), the undersigned, Alex C. Sapir, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

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

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

Date: November 7, 2023	By:	/s/ Alex C. Sapir
		Alex C. Sapir
		President and Chief Executive Officer (Principal Executive Officer)

Exhibit 32.2

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Quarterly Report on Form 10-Q of Fulcrum Therapeutics, Inc. (the "Company") for the period ended September 30, 2023, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Alan Musso, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

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

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

Date: November 7, 2023	By:	/s/ Alan Musso
		Alan Musso
		Chief Financial Officer (Principal Financial Officer)