UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

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

For the quarterly period ended March 31, 2022

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: 001-36644

CALITHERA BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Delaware	**27-2366329**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

343 Oyster Point Blvd., Suite 200
South San Francisco, CA 94080
(Address of principal executive offices including zip code)

Registrant's telephone number, including area code: (650) 870-1000

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, 0.0001 par value	CALA	The Nasdaq Global Select Market

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

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

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

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

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

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

As of May 6, 2022 the registrant had 97,237,262 shares of common stock, $0.0001 par value per share, outstanding.

Calithera Biosciences, Inc.

Quarterly Report on Form 10-Q

For the Quarter Ended March 31, 2022

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PART I. - FINANCIAL INFORMATION
Item 1. Financial Statements

Calithera Biosciences, Inc.
Condensed Consolidated Balance Sheets
(Unaudited)
(In thousands, except per share amounts)

	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 44,664	$ 59,537
Receivable related to asset purchase agreement	127	—
Prepaid expenses and other current assets	2,478	1,915
Total current assets	47,269	61,452
Restricted cash	270	270
Property and equipment, net	492	556
Operating lease right-of-use asset	2,205	2,478
Total assets	$ 50,236	$ 64,756
Liabilities, Convertible Preferred Stock and Stockholders' (Deficit) Equity		
Current liabilities:		
Accounts payable	$ 2,124	$ 3,650
Accrued and other liabilities	9,251	10,356
Total current liabilities	11,375	14,006
Noncurrent operating lease liability	1,295	1,666
Total liabilities	12,670	15,672
Commitments and contingencies		
Convertible preferred stock; $0.0001 par value; 10,000 shares authorized as of March 31, 2022 and December 31, 2021; 1,000 shares issued and outstanding as of March 31, 2022 and December 31, 2021; $35,000 liquidation preference as of March 31, 2022 and December 31, 2021 (Note 7)	40,702	40,702
Stockholders' (deficit) equity:		
Common stock, $0.0001 par value, 200,000 shares authorized as of March 31, 2022, and December 31, 2021; 78,718 and 77,144 shares issued and outstanding as of March 31, 2022, and December 31, 2021, respectively	8	8
Additional paid-in capital	502,017	499,700
Accumulated deficit	(505,161)	(491,326)
Total stockholders' (deficit) equity	(3,136)	8,382
Total liabilities, convertible preferred stock and stockholders' (deficit) equity	$ 50,236	$ 64,756

See accompanying notes.

Calithera Biosciences, Inc.
Condensed Consolidated Statements of Operations
(Unaudited)
(In thousands, except per share amounts)

	Three Months Ended March 31,	
	2022	2021
Operating expenses:		
Research and development	$ 9,566	$ 15,339
General and administrative	4,260	5,428
Total operating expenses	13,826	20,767
Loss from operations	(13,826)	(20,767)
Interest and other income (expense), net	(9)	372
Net loss	$ (13,835)	$ (20,395)
Net loss per share, basic and diluted	$ (0.18)	$ (0.28)
Weighted average common shares used to compute net loss per share, basic and diluted	78,468	72,247

See accompanying notes.

Calithera Biosciences, Inc.
Condensed Consolidated Statements of Comprehensive Loss
(Unaudited)
(In thousands)

	Three Months Ended March 31,	
	2022	2021
Net loss	$ (13,835)	$ (20,395)
Other comprehensive loss:		
Net unrealized loss on available-for-sale securities	—	(3)
Total comprehensive loss	$ (13,835)	$ (20,398)

See accompanying notes.

Calithera Biosciences, Inc.
Condensed Consolidated Statements of Stockholders' (Deficit) Equity
(Unaudited)
(In thousands)

	Three Months Ended March 31, 2022							
	Convertible Preferred Stock		Common Stock					
	Shares	Amount	Shares	Amount	Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' (Deficit) Equity
Balance at December 31, 2021	1,000	$ 40,702	77,144	$ 8	$ 499,700	$ (491,326)	$ —	$ 8,382
Issuance of common stock in connection with at-the-market offering, net of underwriting commissions and issuance costs	—	—	1,234	—	1,137	—	—	1,137
Issuance of common stock pursuant to equity incentive plans	—	—	340	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	1,180	—	—	1,180
Net loss	—	—	—	—	—	(13,835)	—	(13,835)
Balance at March 31, 2022	1,000	$ 40,702	78,718	$ 8	$ 502,017	$ (505,161)	$ —	$ (3,136)

	Three Months Ended March 31, 2021							
	Convertible Preferred Stock		Common Stock					
	Shares	Amount	Shares	Amount	Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Equity
Balance at December 31, 2020	—	$ —	70,686	$ 7	$ 478,599	$ (376,238)	$ 3	$ 102,371
Issuance of common stock in connection with at-the-market offering, net of underwriting commissions and issuance costs	—	—	3,197	—	9,488	—	—	9,488
Exercise of stock options	—	—	1	—	2	—	—	2
Stock-based compensation expense	—	—	—	—	2,695	—	—	2,695
Net loss	—	—	—	—	—	(20,395)	—	(20,395)
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	(3)	(3)
Balance at March 31, 2021	—	$ —	73,884	$ 7	$ 490,784	$ (396,633)	$ —	$ 94,158

See accompanying notes.

Calithera Biosciences, Inc.
Condensed Consolidated Statements of Cash Flows
(Unaudited)
(In thousands)

	Three Months Ended March 31,	
	2022	**2021**
Cash Flows Used in Operating Activities		
Net loss	$ (13,835)	$ (20,395)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	64	73
Accretion of discounts on investments	—	3
Stock-based compensation	1,180	2,695
Gain on remeasurement of the lease liability	—	(362)
Non-cash lease expense	273	351
Changes in operating assets and liabilities:		
Receivables	(127)	513
Prepaid expenses and other current assets	(146)	(619)
Accounts payable	(1,526)	(390)
Accrued liabilities	(1,560)	(3,402)
Lease liability	(333)	(469)
Net cash used in operating activities	(16,010)	(22,002)
Cash Flows Provided by Investing Activities		
Proceeds from sale and maturity of investments	—	6,500
Net cash provided by investing activities	—	6,500
Cash Flows Provided by Financing Activities		
Proceeds from issuance of common stock through an at-the-market offering, net	1,137	9,535
Proceeds from stock option exercises	—	2
Net cash provided by financing activities	1,137	9,537
Net decrease in cash, cash equivalents, and restricted cash	(14,873)	(5,965)
Cash, cash equivalents, and restricted cash at beginning of period	59,807	107,586
Cash, cash equivalents, and restricted cash at end of period	$ 44,934	$ 101,621
Supplemental Disclosure of Non-Cash Activities:		
Unpaid amounts related to stock issuance and deferred financing costs	$ 417	$ 47

See accompanying notes.

1. Organization and Basis of Presentation

Organization

Calithera Biosciences, Inc., or the Company, was incorporated in the State of Delaware on March 9, 2010. The Company is a clinical-stage precision oncology biopharmaceutical company developing targeted therapies to redefine treatment for biomarker-specific patient populations. Driven by a commitment to rigorous science and a passion for improving the lives of people impacted by cancer and other life-threatening diseases, Calithera is advancing a pipeline of investigational, small molecule oncology compounds with a biomarker-driven approach that targets genetic vulnerabilities in cancer cells to deliver new therapies for patients suffering from aggressive hematologic and solid tumor cancers for which there are currently limited treatment options. The Company's principal operations are based in South San Francisco, California, and it operates in one segment.

Presentation

The condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, Calithera Biosciences UK Limited and Calithera Biosciences Ireland Limited. All significant intercompany accounts and transactions have been eliminated from the condensed consolidated financial statements.

The Company's Ability to Continue as a Going Concern

As of March 31, 2022, the Company had cash and cash equivalents of $44.7 million. On April 1, 2022, the Company received $8.5 million in net proceeds from its public offering of shares of its common stock and warrants, after deducting underwriting discounts, commissions and offering costs. The Company has incurred losses since inception and to date has financed its operations primarily through the sale of shares of its capital stock and payments from the Company's collaboration and licensing agreements. As of March 31, 2022, the Company had an accumulated deficit of $505.2 million. During the year ended December 31, 2021 and three months ended March 31, 2022, the Company incurred a loss from continuing operations of $115.1 million and $13.8 million, respectively, and used $66.3 million and $16.0 million of cash in operations, respectively. The Company expects to continue to generate operating losses and negative operating cash flows for the foreseeable future and will need additional funding to support its planned operating activities through profitability. The transition to profitability is dependent upon the successful development, approval, and commercialization of its existing product candidates, including sapanisertib and mivavotinib, and the achievement of a level of revenues adequate to support its cost structure.

In accordance with Accounting Standards Codification, or ASC, 205-40, *Going Concern*, the Company evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about its ability to continue as a going concern within one year after the date that these condensed consolidated financial statements are issued on May 10, 2022. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists under this methodology, management evaluates whether the mitigating effect of its plans sufficiently alleviates substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (1) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued, and (2) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that these condensed consolidated financial statements are issued. In performing its analysis, management excluded certain elements of its operating plan that cannot be considered probable. Under ASC 205-40, the future receipt of potential funding from future equity or debt issuances cannot be considered probable at this time because these plans are not entirely within the Company's control and have not been approved by the board of directors as of the date of these condensed consolidated financial statements.

The Company's expectation to generate operating losses and negative operating cash flows in the future and the need for additional funding to support its planned operations raise substantial doubt regarding the Company's ability to continue as a going concern for a period of one year after the date that these condensed consolidated financial statements are issued on May 10, 2022. Management's plans to alleviate the conditions that raise substantial doubt include the pursuit of additional cash resources through sales of shares of its capital stock, reduced 2022 spending, and potentially through strategic collaboration or licensing agreements. Management has concluded the likelihood that its plan to successfully obtain sufficient funding from one or more of these sources, or adequately reduce expenditures, while reasonably possible, is less than probable. Accordingly, the Company has concluded that substantial doubt exists about the Company's ability to continue as a going concern for a period of at least 12 months from the date of issuance of these condensed consolidated financial statements.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of the uncertainties described above.

2. Summary of Significant Accounting Policies

Unaudited Interim Financial Information

The interim condensed consolidated balance sheet as of March 31, 2022, the statements of operations, comprehensive loss, and stockholders' (deficit) equity, for the three months ended March 31, 2022 and 2021, and the statement of cash flows for the three months ended March 31, 2022 and 2021 are unaudited. The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the annual financial statements and reflect, in the opinion of management, all adjustments of a normal and recurring nature that are necessary for the fair presentation of the Company's condensed consolidated financial statements included in this report. The financial data and the other information disclosed in these notes to the condensed consolidated financial statements related to the three-month period are also unaudited. The results of operations for the three months ended March 31, 2022 are not necessarily indicative of the results to be expected for the year ending December 31, 2022 or for any other future annual or interim period. The balance sheet as of December 31, 2021 included herein was derived from the audited consolidated financial statements as of that date. These condensed consolidated financial statements should be read in conjunction with the Company's audited financial statements included in the Company's Form 10-K as filed with the Securities and Exchange Commission, or SEC.

Use of Estimates

The accompanying condensed consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of condensed consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contract assets and contingent liabilities as of the date of the condensed consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to clinical trial accrued liabilities, revenue recognition, fair value of marketable securities, income taxes, and stock-based compensation. Management bases its estimates on historical experience and on various other market specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Cash and Cash Equivalents

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

Investments

All investments have been classified as "available-for-sale" and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its investments at the time of purchase and reevaluates such designation as of each balance sheet date. As of each balance sheet date, the Company classifies available-for-sale securities with remaining contractual maturities of more than one year as long-term investments, and those with remaining contractual maturities of one year or less as short-term investments. Unrealized gains and losses are excluded from earnings and are reported as a component of comprehensive loss. Realized gains and losses and declines in fair value judged to be other than temporary, if any, on available-for-sale securities are included in interest and other income (expense), net. The cost of securities sold is based on the specific-identification method. Interest on marketable securities is included in interest and other income (expense), net.

Restricted Cash

Restricted cash consists of money market funds held by the Company's financial institution as collateral for the Company's obligations under its facility lease for the Company's corporate headquarters in South San Francisco, California.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents, investments and restricted cash. The Company invests in a variety of financial instruments and, by its policy, limits these financial instruments to high credit quality securities issued by the U.S. government, U.S. government-sponsored agencies and highly rated banks and corporations, subject to certain concentration limits. The Company's cash, cash equivalents, investments and restricted cash are held by financial institutions in the United States that management believes are of high credit quality. Amounts on deposit may at times exceed federally insured limits.

Revenue Recognition

The Company records revenue in accordance with Accounting Standards Codification, or ASC No. 2014-09, *Revenue from Contracts with Customers (Topic 606)*, or ASC 606. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company has a collaboration and license agreement with Incyte, the Incyte Collaboration Agreement, and a license agreement with Antengene, the Antengene License Agreement, that are within the scope of ASC 606, under which the Company licenses certain rights to its product candidates. The terms of these arrangements include payment to the Company of non-refundable, upfront license fees, and potential development, regulatory and sales milestones, and sales royalties. Each of these payments results in collaboration or license revenue, except for revenues from royalties on net sales of licensed products, which would be classified as royalty revenues.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under its agreement, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract.

Licenses of Intellectual Property: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from non-refundable, upfront fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promised goods or services, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, upfront fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone Payments: At the inception of each arrangement that includes development, regulatory or commercial milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant reversal of cumulative revenue would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received or the underlying activity has been completed. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue in the period of adjustment.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

Contract Balances

Upfront payments and fees are recorded as deferred revenue upon receipt or when due, and may require deferral of revenue recognition to a future period until the Company performs its obligations under these arrangements. Amounts payable to the Company are recorded as accounts receivable when the Company's right to consideration is unconditional.

The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less.

The Company had no contract assets or liabilities as of March 31, 2022 and December 31, 2021. For the three months ended March 31, 2022 and 2021, the Company did not recognize any revenue from performance obligations satisfied in previous periods.

Awards

The Company assesses at the inception of award agreements whether the agreement is a liability. If the Company is obligated to repay funds received regardless of the outcome of the related research and development activities, then the Company is required to estimate and recognize a liability for this obligation. Alternatively, if the Company is not required to repay the funds, then payments received are recorded as contra research and development expense in the consolidated statement of operations as expenses are incurred. If payment criteria has been met and allowable expenses have been incurred, but not received at the balance sheet date, the amount of the receivable is included in receivables from collaborations in the consolidated balance sheet.

Accrued Research and Development Costs

The Company records accrued liabilities for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of preclinical and clinical studies, and contract manufacturing activities. The Company records the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and includes these costs in accrued and other liabilities in the consolidated balance sheets and within research and development expense in the consolidated statements of operations. These costs are a significant component of the Company's research and development expenses. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers under the service agreements. The Company makes significant judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become known, the Company adjusts its accrued liabilities. The Company has not experienced any material differences between accrued costs and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled, and the rate of patient enrollments may vary from the Company's estimates, resulting in adjustments to expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations.

Leases

The Company accounts for its leases under ASC No. 2016-02, *Leases (Topic 842)*, or ASC 842. Operating lease right-of-use, or ROU, assets and lease liabilities are recognized at commencement and are recorded for leases with durations greater than 12 months.

ROU assets represent the Company's right to use an underlying asset during the lease term, and lease liabilities represent the Company's obligation to make lease payments arising from the lease. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that it will exercise that option. Operating lease ROU assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. The Company estimates an incremental borrowing rate based on the information available at commencement date, in determining the present value of lease payments. The operating lease ROU asset also includes lease incentives. Lease expense is recognized on a straight-line basis over the lease term. The Company elected to not separate lease components and non-lease components for its long-term facility lease. Variable lease payments include lease operating expenses.

Stock-Based Compensation

The Company maintains various stock incentive plans under which stock options and restricted stock awards are granted to employees, non-employee directors of the board, and non-employees. The Company also has an employee stock purchase plan for all eligible employees. Stock options and stock purchased under the employee stock purchase plan, are recorded at fair value as of the grant date using the Black-Scholes option-pricing model. Restricted stock awards are measured at grant date fair value, at the market price of the Company's common stock on the grant date. The Company has elected to account for forfeitures as they occur. The Company records stock-based compensation expense related to the service-based instruments ratably over the employee, director, or non-employees' respective requisite service period (generally the vesting period). For performance-based stock awards with vesting conditioned on the achievement of certain strategic milestones, stock-based compensation expense is recognized over the period from the date the performance condition is determined to be probable of occurring through the date the applicable condition is expected to be met. If the performance condition is not considered probable of being achieved, no stock-based compensation expense is recognized until such time as the performance condition is considered probable of being met, if at all. If the assessment of the probability of the performance condition being met changes, the impact of the change in estimate would be recognized in the period of the change.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding during the period without consideration of common stock equivalents. Since the Company was in a loss position for all periods presented, basic net loss per share is the same as diluted net loss per share for all periods as the inclusion of all potential common shares outstanding would have been anti-dilutive.

Accounting Pronouncement Not Yet Adopted

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, or ASU 2016-13. The updated accounting guidance requires changes to the recognition of credit losses on financial instruments not accounted for at fair value through net income. In May 2019, the FASB issued ASU No. 2019-05, *Targeted Transition Relief*, which provides transition guidance to entities that elect the fair value option for eligible instruments. In November 2019, the FASB issued ASU 2019-10 which extends the effective date of the standards for smaller reporting companies to interim and annual periods beginning after December 15, 2022. These standards require using a modified retrospective approach with the cumulative effect recognized as an adjustment to retained earnings. A prospective transition approach is required for debt securities that have recognized an other-than-temporary impairment prior to the effective date. For the Company's receivables from collaborations and other agreements and certain other financial instruments, the Company will be required to use a forward-looking "expected" credit loss model instead of the existing "incurred" credit loss model, which will generally result in earlier recognition of allowances for credit losses. The Company plans to adopt this standard effective January 1, 2023. The Company is currently evaluating the effect the guidance will have on its financial statements or disclosures.

3. Fair Value Measurements

Fair value accounting is applied for all financial assets and liabilities that are recognized or disclosed at fair value in the condensed consolidated financial statements on a recurring basis (at least annually). Financial instruments include cash and cash equivalents, investments, receivables, accounts payable, and accrued liabilities that approximate fair value due to their relatively short maturities.

Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The authoritative guidance on fair value measurements establishes a three tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

A financial instrument's categorization within the valuation hierarchy is based upon the lowest level of input that is significant to the fair value measurement. Where quoted prices are available in an active market, securities are classified as Level 1. The Company classifies money market funds as Level 1. When quoted market prices are not available for the specific security, then the Company estimates fair value by using quoted prices for identical or similar instruments in markets that are not active and model-based valuation techniques for which all significant inputs are observable in the market or can be corroborated by observable market data for substantially the full term of the assets. Where applicable, these models project future cash flows and discount the future amounts to a present value using market-based observable inputs obtained from various third party data providers, including but not limited to, benchmark yields, interest rate curves, reported trades, broker/dealer quotes and market reference data. The Company classifies its corporate notes and U.S. government agency securities as Level 2. Level 2 inputs for the valuations are limited to quoted prices for similar assets or liabilities in active markets and inputs other than quoted prices that are observable for the asset or liability.

The following table sets forth the fair value of our financial assets and liabilities, allocated into Level 1, Level 2 and Level 3, that were measured on a recurring basis (in thousands):

	March 31, 2022			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 43,944	$ —	$ —	$ 43,944
Total financial assets	$ 43,944	$ —	$ —	$ 43,944

	December 31, 2021			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 56,337	$ —	$ —	$ 56,337
Total financial assets	$ 56,337	$ —	$ —	$ 56,337

4. Financial Instruments

Cash equivalents and investments, all of which are classified as available-for-sale securities and restricted cash, consisted of the following (in thousands):

	March 31, 2022				December 31, 2021			
	Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value	Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value
Money market funds	$ 43,944	$ —	$ —	$ 43,944	$ 56,337	$ —	$ —	$ 56,337
	$ 43,944	$ —	$ —	$ 43,944	$ 56,337	$ —	$ —	$ 56,337
Classified as:								
Cash equivalents				$ 43,674				$ 56,067
Restricted cash				270				270
Total cash equivalents, restricted cash and investments				$ 43,944				$ 56,337

There have been no significant realized gains or losses on available-for-sale securities for the periods presented. As of March 31, 2022 and December 31, 2021, there were no unrealized losses on cash equivalents. As of March 31, 2022, the Company had a total of $44.9 million in cash, cash equivalents and restricted cash, which includes approximately $1 million in cash and $43.9 million in cash equivalents and restricted cash.

5. Accrued and Other Liabilities

Accrued and other liabilities consist of the following (in thousands):

	March 31, 2022	December 31, 2021
Accrued clinical and manufacturing expenses	$ 4,202	$ 5,086
Accrued payroll and related expenses	2,146	3,283
Current portion of lease liability	1,412	1,374
Accrued professional and consulting expenses	977	155
Other	514	458
Total accrued and other liabilities	$ 9,251	$ 10,356

6. Leases

The Company has a non-cancelable facility lease agreement, or the Lease, for office and laboratory facilities in South San Francisco, California, with a remaining lease term of 1.8 years, through January 2024, and a two-year renewal option prior to expiration. The renewal option to extend the Lease was not considered in the determination of the right-of-use asset or the lease liability for the Lease as the Company did not consider it reasonably certain that it would exercise any such option. The Lease provides that the Company is obligated to pay certain variable costs, including taxes and operating expenses. The Lease is classified as an operating lease. From inception, the Company measured the present value of its lease liability using an estimated incremental borrowing rate of 9%.

On March 8, 2021, the Company amended its lease to reduce its rentable area from approximately 54,000 square feet to approximately 34,000 square feet. The related reduction in rent was effective January 1, 2021. In connection with the amendment, the Company also reduced its existing letter of credit from $440,000 to $270,000 as a security deposit to the lease. Subsequent to the amendment, which was determined to be a modification of the lease, the Company remeasured the present value of its lease liability using an estimated incremental borrowing rate of 7.5%. The Company recognized a gain of $0.4 million, which is included in interest and other income (expense), net in its unaudited condensed consolidated statement of operations for the three months ended March 31, 2021, which represents the difference between the reduced lease liability and the reduction in the operating lease right of use asset.

The components of net operating lease costs included in the condensed consolidated statement of operations for the three months ended March 31, 2022 and 2021, were as follows (in thousands):

	Three Months Ended March 31,	
Operating Lease Costs:	**2022**	**2021**
Straight-line rent expense related to facility operating lease	$ 326	$ 484
Variable rent expense related to facility operating lease	229	244
Net operating lease costs	$ 555	$ 728

Cash paid for amounts included in the measurement of the lease liabilities for both the three months ended March 31, 2022 and 2021, was $0.4 million and $0.6 million, respectively, was included in net cash used in operating activities in the Company's unaudited condensed consolidated statements of cash flows.

The balance sheet classification of the Company's operating lease liability was as follows (in thousands):

Operating Lease Liability:	March 31, 2022	December 31, 2021
Current portion included in accrued and other liabilities	$ 1,412	$ 1,374
Noncurrent operating lease liability	1,295	1,666
Total operating lease liability	$ 2,707	$ 3,040

The maturities of the Company's lease liability as of March 31, 2022, was as follows (in thousands):

Year ending December 31:	
2022 (excluding the three months ended March 31, 2022)	$ 1,161
2023	1,593
2024	136
Total lease payments	2,890
Less: interest	(183)
Present value of lease liability	$ 2,707

7. Takeda Asset Purchase and Stock Purchase Agreements

Takeda Asset Purchase Agreement

On October 18, 2021, the Company entered into an Asset Purchase Agreement, or APA, with Millennium Pharmaceuticals, Inc. or Millennium, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, or Takeda, pursuant to which the Company acquired and licensed from Millennium certain technology, intellectual property and other assets related to Takeda's small molecule programs sapanisertib (CB-228, formerly known as TAK-228) and mivavotinib (CB-659, formerly known as TAK-659), or the Takeda Programs.

Under the APA, Millennium assigned or caused to be assigned to the Company certain patents and know-how solely related to the Takeda Programs and necessary for the exploitation of products containing the CB-228 and CB-659 compounds, as well as specified regulatory materials, agreements, materials and inventory related to the Takeda Programs. Takeda also granted to the Company a license under certain other intellectual property necessary for the exploitation of such products. The Company granted to Millennium a license under the intellectual property assigned by Takeda to the Company (including intellectual property controlled by the Company via the assigned contracts) in order for Millennium to perform its obligations under the APA, ancillary agreements executed in connection with the APA and other retained agreements and for Millennium's internal research use.

The Company must use commercially reasonable efforts to develop and commercialize at least one CB-228 product and one CB-659 product in each of the United States, Japan and certain European countries.

Pursuant to the APA, in October 2021, the Company paid Millennium an upfront payment of $10 million in cash and issued to Millennium 1,000,000 shares of its Series A convertible preferred stock as referenced below. In determining the total purchase consideration paid to Millennium, the Series A convertible preferred stock shares were classified as level 3 in the valuation hierarchy due to the presence of significant unobservable inputs, and were valued upon issuance at $40.9 million using the Black-Scholes option-pricing model and the following assumptions:

		Description
Credit spread	12.4%	Allowance for counterparty credit risk of the Company given the liquidation preference and obligation to issue more shares as the stock price decreases
Probability of a Qualified Financing	75%	As determined upon issuance date
Expected timing of a Qualified Financing	0.5 years	As determined upon issuance date
Expected term	0.7 years	Weighted average of time to a Qualified Financing and time to the Mandatory Pricing Date, as determined upon issuance date
Volatility	55%	Based on the Company's trading history for its common stock over the estimated term to the mandatory pricing date
Risk-free interest rate	0.08%	Based on the U.S. constant maturity treasury yield curve at the time of issuance over the expected term
Common stock price	$2.04	The Company's closing common stock price on October 15, 2021

Total consideration transferred was $50.9 million and was comprised of the $10 million cash payment and the estimated fair value of the shares of the Company's Series A convertible preferred stock of $40.9 million. The Company recorded a charge of $50.9 million related to the assets acquired to "research and development related to asset acquisition" in the consolidated statements of operations as the assets acquired had no alternative future use at the time of the acquisition. There were no material direct transaction costs related to the transaction.

The Company will make tiered earn-out payments of high single-digits to low teens on net sales of CB-228 products and CB-659 products, subject to certain customary reductions. Millennium will be eligible to receive up to an aggregate of $470 million in clinical development, regulatory and sales milestone payments across both Takeda Programs.

The term of the APA will continue until the expiration of the Company's obligations to make earn-out payments, unless earlier terminated. Either party may terminate the APA in the event of an uncured material breach of the other party or in the case of insolvency of the other party.

Preferred Stock Purchase Agreement

On October 18, 2021, in accordance with the APA, the Company entered into a Preferred Stock Purchase Agreement, or the Purchase Agreement, with Millennium, pursuant to which it agreed to issue 1,000,000 shares of its Series A convertible preferred stock, or the Series A preferred stock. Each share of Series A preferred stock is initially convertible at the option of the holder into approximately 17.2 shares of common stock, based on the Company's $2.04 per share closing stock price on October 15, 2021. The conversion rate of the Series A preferred stock is subject to anti-dilution adjustments that if triggered would result in the issuance of additional shares of common stock upon conversion.

The holder of the Series A preferred stock has the following rights, preferences and privileges:

Voting Rights

The holder of Series A preferred stock will be entitled to cast the number of votes equal to the number of whole shares of common stock into which the shares of Series A preferred stock are convertible on any matter presented to the stockholders of the Company or at any meeting of stockholders, subject to certain beneficial ownership limitations.

Additionally, certain matters require the approval of the Series A preferred stock, voting as a separate class, including to (i) amend the Company's organizational documents in a way that has an adverse effect on the Series A preferred stock, (ii) create or authorize the creation of any new security, or reclassify or amend any existing security, of the Company that are senior to, or equal in priority with, the Series A preferred stock, including any shares of Series A preferred stock, with respect to the distribution of assets on the liquidation, dissolution or winding up of the Company, the payment of dividends and rights of redemption or (iii) purchase or

redeem, or pay or declare, any dividend or make any distribution on, any shares of capital stock of the Company, subject to certain exceptions.

Mandatory Conversion

The Series A preferred stock will automatically convert, subject to certain beneficial ownership limitations, on the earlier of (i) the 18-month anniversary of the date of issuance, or the Mandatory Pricing Date, into 17,156,863 shares of common stock, subject to adjustment into additional shares of common stock if the volume weighted-average price of common stock on the thirty (30) trading days prior to the Mandatory Pricing Date is lower than $2.04 and (ii) a qualified financing that results in net proceeds to the Company of at least $40 million, excluding the conversion of the Series A preferred stock into 17,156,863 shares of common stock, subject to adjustment into additional shares of common stock if the weighted-average price paid by investors in the Qualified Financing is lower than $2.04 per share.

Optional Conversion

The Series A preferred stock is convertible, subject to certain beneficial ownership limitations, at the option of the holder thereof, at any time prior to the Mandatory Pricing Date or a Qualified Financing into 17,156,863 shares of common stock, subject to adjustment into additional shares of common stock if the volume weighted-average sales price per share of certain shares of common stock sold from the issuance date of the Series A preferred stock through the date of the election to convert is lower than $2.04 per share.

Dividends

The Series A preferred stock will be entitled to dividends or distributions on shares of Series A preferred stock equal to and in the same form as dividends or distributions actually paid on shares of the common stock when, as and if such dividends or distributions are paid. No dividends had been declared by the Board of Directors as of March 31, 2022.

Liquidation Preference

The Series A preferred stock will have preference over the common stock with respect to distribution of assets or available proceeds, as applicable, in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or any other deemed liquidation event, and will be entitled to a liquidation preference equal to the greater of the original issuance price of the Series A preferred stock and the payment such holder would have received had the Series A preferred stock been converted into shares of common stock immediately prior to such liquidation event.

Redemption Rights

The holders of the Series A preferred stock have no redemption rights. However, if the Company is unable to obtain stockholder approval, and as a result the Series A preferred stockholders are unable to convert all the shares into common stock, then the parties shall promptly negotiate in good faith the timing and amount per share to be paid to compensate the holder for such inability (“Redemption Event”); provided, however that the Company shall not be required to make any cash redemption payment until at least three years after the Closing Date without the Company’s consent.

The Company has recorded the Series A preferred stock at an estimated fair value at the time of issuance of $40.9 million, net of issuance costs of approximately $0.2 million. The Company has classified the Series A preferred stock as temporary equity due to the uncertainty of having sufficient authorized common stock reserved for issuance to cover the potential conversion of the Series A preferred stock into common stock if any of the conversion features (optional or automatic) are triggered.

If the Company does not receive the Requisite Stockholder Approval, then the Company may be required to compensate the holder, upon occurrence of a Redemption Event. At the end of each reporting period, the Company adjusts the Series A preferred stock carrying value to the greater of the issuance date fair value of $40.9 million or the current redemption amount in accordance with ASC 480-10-S99-3A, *Distinguishing Liabilities from Equity.* As March 31, 2022, the Series A preferred stock was recorded at $40.9 million.

8. Stockholders' (Deficit) Equity

At-the-Market Offering

In August 2020, the Company entered into a sales agreement with Jefferies as sales agent and underwriter, pursuant to which the Company could issue and sell shares of its common stock with an aggregate maximum offering price of $75 million under an at-the-market offering program, or the ATM program. The Company will pay Jefferies up to 3% of gross proceeds for any common stock sold through the sales agreement. During the three months ended March 31, 2022, the Company sold 1,233,875 shares under the ATM program at an average price per share of $0.57, for net proceeds of $0.7 million, and received $0.4 million upon the settlement of trades outstanding at December 31, 2021. As of March 31, 2022, a total of 6,479,285 shares had been sold under the ATM program.

9. Stock-Based Compensation

Stock Options

A summary of stock option activity was as follows (in thousands, except weighted-average exercise price and contractual term amounts):

	Options Outstanding			
	Number of Shares Underlying Outstanding Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding — December 31, 2021	8,324	$ 6.18		
Options granted	2,294	$ 0.44		
Options cancelled	(901)	$ 6.63		
Outstanding — March 31, 2022	9,717	$ 4.78	6.73	$ —
Exercisable — March 31, 2022	5,339	$ 6.77	5.40	$ —

Stock Awards

During the three months ended March 31, 2022, the Company issued 9,200 restricted stock units, or RSUs, to its employees. The RSUs vest 25% annually over 4 years commencing on the date of grant. The RSUs are measured at grant date fair value, at the market price of the Company's common stock on the grant date. The Company records stock-based compensation expense related to the RSUs ratably over the employee respective requisite service period.

On January 20, 2021, the Company granted 1,607,812 performance-based restricted stock units, or PSUs, to employees. The PSUs vested 20% on January 3, 2022 and 80% upon the achievement of two goals that were achieved by January 3, 2022. The PSUs were measured at grant date fair value, using the market price of the Company's common stock on the grant date of $2.98. The Company estimated that all vesting conditions were probable of being achieved and elected to recognize compensation expense for the PSUs as one aggregate award using the straight-line method over the estimated implicit service period from the grant date to January 3, 2022. The Company monitored the probability of achievement of the goals each reporting period and adjusted its estimates accordingly. During the three months ended March 31, 2022 and 2021, the Company recorded $6,000 and $0.9 million of expense, respectively, related to the PSUs.

A summary of restricted stock unit activity was as follows (in thousands, except weighted-average grant-date fair value and contractual term amounts):

	Stock Awards (PSUs and RSUs)			
	Shares	Weighted-Average Grant-Date Fair Value	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding — December 31, 2021	716	$ 2.86		
RSUs — Awarded	9	$ 0.65		
PSUs and RSUs — Vested	(340)	$ 2.98		
PSUs and RSUs — Cancelled	(15)	$ 2.85		
Outstanding — March 31, 2022	370	$ 2.70	1.84	$ 150

Total stock-based compensation expense related to the Company's 2010 Equity Incentive Plan, 2014 Equity Incentive Plan, 2018 Inducement Plan, and the 2014 Employee Stock Purchase Plan was as follows (in thousands):

	Three Months Ended March 31,	
	2022	2021
Research and development	$ 498	$ 1,280
General and administrative	682	1,415
Total stock-based compensation	$ 1,180	$ 2,695

10. Net Loss per Share

Since the Company was in a loss position for all periods presented, diluted net loss per share is the same as basic net loss per share for all periods as the inclusion of all potential common shares outstanding would have been anti-dilutive.

Potentially dilutive securities that were not included in the diluted net loss per share calculations because they would be anti-dilutive were as follows (in thousands):

	March 31,	
	2022	2021
Options to purchase common stock	9,717	9,436
Employee stock plan purchases	137	42
Restricted stock units subject to future vesting	370	2,048
Conversion of Series A preferred stock into shares of common stock	17,157	—
Total	27,381	11,526

11. Collaboration and Licensing Agreements

Incyte Collaboration and License Agreement

On January 27, 2017, the Company entered into a collaboration and license agreement with Incyte, or the Incyte Collaboration Agreement. Under the terms of the Incyte Collaboration Agreement, the Company granted Incyte an exclusive, worldwide license to develop and commercialize its small molecule arginase inhibitors for hematology and oncology indications. Through September 30, 2020, the parties collaborated on and co-funded the development of the licensed products, with Incyte bearing 70% and the Company bearing 30% of global development costs. The parties would share profits and losses in the United States, with 60% to Incyte and 40% to the Company. The Company would have the right to co-detail the licensed products in the United States, and Incyte would pay the Company tiered royalties ranging from the low to mid-double digits on net sales of licensed products outside the United States.

The Incyte Collaboration Agreement also provides that the Company may choose to opt out of its co-funding obligations at any time. On August 28, 2020, the Company delivered written notice to Incyte of its decision to opt out of its co-development rights effective September 30, 2020. As a result of the Company's decision to opt out, Incyte will pay all costs to develop INCB001158 or any other licensed products. In addition, the Company's rights to U.S. profit sharing will no longer be in effect, and instead Incyte will pay Calithera tiered royalties ranging from the low double digits to mid-teens on net sales of licensed products in the U.S., an incremental 3% royalty on annual net sales in the United States of such licensed product until such incremental royalty equals 120% of previous development expenditures incurred by the Company.

Under the Incyte Collaboration Agreement, the Company received an upfront payment of $45 million in February 2017. In March 2017, the Company achieved a development milestone of $12 million, for which the Company received payment in May of 2017. In April 2020, the Company filed a complaint against Incyte in the Superior Court of California, San Francisco County, asserting claims for breach of contract arising out of Incyte's failure to pay two milestone payments totaling $18 million the Company believed were due under the Incyte Collaboration Agreement. In September 2021, the Company entered into a Settlement Agreement and Release with Incyte. Concurrently, the parties also filed a dismissal of the complaint in the Superior Court of California. Under the terms of the Settlement Agreement and Release, which resolves all claims in the complaint without any admission of liability or fault, Incyte was to pay the Company a negotiated settlement amount of $6.75 million and the parties have exchanged mutual releases. In September 2021, the Company received and recognized the $6.75 million as milestone revenues. Total remaining potential development, regulatory and commercialization milestones as of March 31, 2022 were $720 million.

The Incyte Collaboration Agreement is considered to be under the scope of ASC Topic 808, *Collaborative Arrangements*. The Company has concluded that the research and development co-funding activities were not representative of a customer relationship

and this unit of account is accounted for as an increase to or reduction of research and development expenses, rather than as revenue. In addition, the Company has analogized to ASC 606 for other aspects of the arrangement. The performance obligations under the Incyte Collaboration Agreement consist of intellectual property licenses and the performance of certain manufacturing and manufacturing technology transfer services. The Company determined that the license is not distinct from the associated manufacturing and technology transfer services to be performed under the agreement. Specifically, the Company believes the license is not capable of being distinct, as Incyte did not have the know-how to manufacture the collaboration product without Calithera's assistance until completion of the manufacturing technology transfer process, and no other third parties could perform such assistance due to the early stage nature of the licensed intellectual property as well as Calithera's propriety knowledge with respect to the licensed intellectual property.

Net costs associated with co-development activities performed under the Incyte Collaboration Agreement are included in research and development expenses in the accompanying consolidated statements of operations, with any reimbursement of costs by Incyte reflected as a reduction of such expenses. For the three months ended March 31, 2022 and 2021, net costs payable to Incyte were approximately $29,000 and $0.7 million, respectively. As of March 31, 2022, net amounts payable to Incyte were $0.7 million.

Antengene License Agreement

On May 16, 2021, the Company entered into a license agreement, or the Antengene License Agreement, with Antengene Investment, Ltd., a wholly-owned subsidiary of Antengene Corporation. Under the terms of the Antengene License Agreement, the Company granted Antengene an exclusive, worldwide license to develop and commercialize CB-708, the Company's small molecule inhibitor of CD73. The Company received an upfront payment of $3 million in May 2021 and may receive potential development, regulatory and sales milestones of up to $252 million, as well as tiered royalties on sales of the licensed product up to low double-digits.

The Antengene License Agreement is considered to be under the scope of ASC 606. In accordance with ASC 606, the Company determined the transaction price to be the $3.0 million upfront payment. The performance obligations consist of the intellectual property license, inventory, and manufacturing technical support services. The transaction price was allocated to the performance obligations on a relative selling price basis, with the value of the manufacturing technical support services considered to be de minimis. The Company determined that it had satisfied the intellectual property license and inventory performance obligations in the second quarter of 2021 and accordingly recognized license revenue of $3 million during the three months ended June 30, 2021. No additional revenue was recognized in subsequent periods related to the Antengene License Agreement.

Symbioscience License Agreement

In December 2014, the Company entered into an exclusive license agreement with Mars, Inc., by and through its Mars Symbioscience division, or Symbioscience, under which the Company has been granted the exclusive, worldwide license to develop and commercialize Symbioscience's portfolio of arginase inhibitors for use in human healthcare, or the Symbioscience License Agreement. There were no expenses related to its licensing arrangement with Mars Symbioscience recorded in the three months ended March 31, 2022 or 2021.

The Company may make future payments of up to $23.6 million contingent upon attainment of various development and regulatory milestones and $95.0 million contingent upon attainment of various sales milestones. Additionally, the Company will pay royalties on sales of the licensed product, if such product sales are ever achieved. If the Company develops additional licensed products, after achieving regulatory approval of the first licensed product, the Company would owe additional regulatory milestone payments and additional royalty payments based on sales of such additional licensed products.

12. Cystic Fibrosis Foundation Development Award

In October 2020, the Company was awarded $2.4 million from the Cystic Fibrosis Foundation, or CFF, to support the clinical development of CB-280 in cystic fibrosis. The award will be paid in installments upon the achievement of certain milestones. The Company recognizes the CFF milestones awards as a reduction to research and development expenses in the accompanying unaudited consolidated statements of operations in the period the milestone is achieved and expenses have been incurred. For the three months ended March 31, 2022 and 2021, no amounts from the CFF were recognized as a reduction of research and development expenses.

The award contains provisions where the Company must repay up to two times the award if it ceases to use commercially reasonable efforts to develop CB-280. Upon commercialization, the Company will owe certain royalty payments to the CFF up to a royalty cap. The Company may also be obligated to make a payment to CFF if the Company transfers, sells or licenses a product in the cystic fibrosis field, or if the Company enters into a change of control transaction. In May 2022, the Company made the decision to no longer pursue further development of CB-280 in cystic fibrosis at this time.

13. Subsequent Event

Public Offering

On April 1, 2022, the Company closed an underwritten public offering of 18,518,519 shares of its common stock at a combined price to the public of $0.54 per share and accompanying common warrants, or $10 million in gross proceeds, resulting in $8.5 million of net proceeds after deducting underwriting discounts, commissions and offering costs. Each share of common stock is accompanied by a warrant to purchase one share of common stock at an exercise price of $0.54 per share, which is immediately exercisable and will expire 18 months from the date of issuance, or a short-term warrant, and a warrant to purchase one share of common stock at an exercise price of $0.54 per share, which is immediately exercisable and will expire 5 years from the date of issuance, or a long-term warrant.

Item 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our unaudited condensed consolidated financial statements and related notes included in Part I, Item 1 of this report.

This Quarterly Report on Form 10-Q contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Forward-looking statements are identified by words such as "believe," "will," "may," "estimate," "continue," "anticipate," "intend," "should," "plan," "expect," "predict," "could," "potentially" or the negative of these terms or similar expressions. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other "forward-looking" information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in this report in Part II, Item 1A — "Risk Factors," and elsewhere in this report. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. These statements, like all statements in this report, speak only as of their date, and we undertake no obligation to update or revise these statements in light of future developments. We caution investors that our business and financial performance are subject to substantial risks and uncertainties. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this Quarterly Report on Form 10-Q. While we believe that information provides a reasonable basis for these statements, that information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into or review of, all relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely on these statements.

Overview

We are a fully-integrated, clinical stage precision oncology biopharmaceutical company. Driven by a commitment to rigorous science and a passion for improving the lives of people impacted by cancer and other life-threatening diseases, we are advancing a pipeline of investigational, small molecule oncology compounds with a biomarker-driven approach.

Targeted, Biomarker-Defined Small Molecules

Our core expertise is in oncology, discovering and developing novel small molecule enzyme inhibitors. We are well-versed and nimble in conducting biomarker-driven early and late stage clinical trials, and are leveraging this expertise by developing the mid-stage clinical assets we have recently added to our precision oncology pipeline.

In October 2021, we entered into an Asset Purchase Agreement, or APA, with Millennium Pharmaceuticals, Inc., or Millennium, a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited, or Takeda, to acquire two clinical-stage compounds, both of which have demonstrated single-agent clinical activity in biomarker-defined cancer patient populations. The compounds are the TORC1/2 inhibitor sapanisertib (CB-228) and the spleen tyrosine kinase (SYK) inhibitor mivavotinib (CB-659), both of which significantly strengthen our precision oncology pipeline. This was a transformative transaction that aligns with Calithera's focus and deep expertise in targeted, small-molecule cancer therapies. Our near-term clinical development plans are to leverage our expertise in conducting biomarker focused clinical trials by developing sapanisertib in NRF2 (also known as NFE2L2)-mutated squamous non-small cell lung cancer, and mivavotinib in activated B-cell (ABC), or non-GCB, diffuse large B-cell lymphoma (DLBCL) with and without MYD88/CD79b mutations. By focusing on well-characterized genetic vulnerabilities with molecules that have already shown single-agent activity, we will be able to generate phase 2 data with targeted, efficient study designs and design potential paths for rapid approval in genetically-defined patient populations. We intend to announce data from these studies by the first quarter of 2023.

SYK Inhibitor Mivavotinib (CB-659)

DLBCL is the most common form of lymphoma, representing approximately 30% of all NHL diagnoses. Approximately 24,000 people are diagnosed with DLBCL in the US each year, with approximately a 60% five-year survival rate. DLBCL treatments are the same for all patients, despite the fact that it is a biologically heterogeneous disease with different cell-of-origin: approximately 40% GCB, approximately 50% ABC and approximately 10% unclassified. DLBCL cell-of-origin is routinely collected at the time of initial diagnosis, using an immunohistochemistry (IHC) assay called the Hans algorithm, which classifies tumors as GCB or non-GCB. Currently, R-CHOP (rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone) is the standard of care for newly diagnosed DLBCL patients. While a fraction of patients will go into remission following R-CHOP, 40-50% of patients relapse or are refractory to R-CHOP. For those patients, the options are salvage chemotherapy, stem cell transplant, and more recent entrants to the treatment landscape such as chimeric antigen receptor-T cell therapy (CAR-T), antibody drug conjugates like polatuzumab and

loncastuximab, and other drugs like tafasitamab and selinexor. However, high unmet need remains for patients who are ineligible for, or relapse after, CAR-T, stem cell transplant, or other salvage therapies. Currently, there are no defined patient selection strategies to optimize therapy for patients in the relapsed or refractory setting. Patients with ABC DLBCL have a poorer prognosis than others; they have fewer curative responses to R-CHOP and shorter median overall survival, or OS. Currently there are no approved treatments specifically for non-GCB (ABC) DLBCL patients.

Mivavotinib is a SYK inhibitor that targets the constitutively activated B-cell receptor, or BCR, pathway in DLBCL and other non-Hodgkin lymphomas, or NHL, and has durable single agent responses in unselected relapsed/refractory DLBCL. Clinical data show mivavotinib is differentiated from other SYK inhibitors, as it showed substantially higher single agent response rates than other SYK inhibitors, which had monotherapy response rates of less than 10 percent in similar DLBCL patient populations. In separate preclinical experiments, mivavotinib showed high tissue distribution, a large volume of distribution, and high tumor:plasma exposure ratio. Therefore, the greater clinical activity seen with mivavotinib than with other SYK inhibitors could be due to higher tissue penetration and duration of target engagement.

The safety profile of mivavotinib is favorable for development as a monotherapy or in combination with other drugs. Over 300 patients with hematologic malignancies have been treated with mivavotinib, with a wide range of well-tolerated, therapeutically efficacious doses. The most common adverse events with mivavotinib monotherapy in NHL patients were asymptomatic and reversible laboratory abnormalities. Mivavotinib is also combinable with bendamustine-rituximab, ibrutinib, and R-CHOP, as demonstrated by prior studies.

SYK is known to activate multiple cell-signaling pathways in activated B-cell like (ABC) DLBCL including NF-kB and phosphoinositide 3-kinase (PI3K) pathways, compared to germinal center B-cell like (GCB) DLBCL, where it primarily activates the PI3K pathway. We conducted a retrospective analysis and found a substantially higher response rate in non-GCB (ABC) of 53% compared to GCB at 22%. In addition, recent preclinical studies have shown enhanced SYK activity, and sensitivity to SYK inhibition in DLBCL with mutations in MyD88 and/or CD79, and this subset of ABC patients are known to have poorer outcomes to standard of care therapies. Approximately 50% of all ABC DLBCL tumors have one or both of these mutations. The compelling single agent ORR in non-GCB (ABC) DLBCL, and potential for further enrichment of in a genetically-defined subset of ABC DLBCL with MyD88/CD79 mutations provide a well-defined, efficient development path.

Based on the combined clinical and preclinical data, we designed a two-part phase 2 trial of mivavotinib in relapsed or refractory non-GCB (ABC) DLBCL with enrichment of MYD88/CD79b mutated tumors using liquid NGS testing. The phase 2a portion of the study will confirm activity in the biomarker-defined subsets and further refine dose/schedule. The trial will enroll non-GCB (ABC) DLBCL patients based on Hans algorithm, and MyD88 and CD79 mutation status will be collected using ctDNA based liquid NGS to accrue a pre-specified number of patients harboring MyD88 or CD79b mutations. Patients will be randomized to either a standard dosing schedule of 100mg QD or an induction dosing schedule of 120mg QD for 14 days, followed by 80mg QD. First patient in, or FPI, is anticipated to be in the second quarter of 2022. We intend to announce data from this study by the first quarter of 2023. Data from Phase 2a will inform Phase 2b, which could be registration-enabling and could potentially enroll expansion cohorts comprised of non-GCB (ABC) DLBCL and MyD88 and/or CD79m DLBCL, with a primary endpoint of ORR to target accelerated approval as a single agent in these biomarker-defined subsets.

While the single agent biomarker-defined phase 2 may provide an initial indication in R/R non-GCB (ABC) DLBCL and/or MYD88/CD79b mutated DLBCL, there will be future opportunities to pursue combination strategies with novel and/or standard-of-care therapies to expand development in earlier lines of therapy in DLBCL. Additional paths for monotherapy and combination development include Waldenstrom's Macroglobulinemia (which has a 95% prevalence of MYD88 mutation), a biomarker-defined subset of GCB DLBCL, and other indolent lymphomas where mivavotinib has shown compelling single agent responses in completed trials. Lastly, based on its dual SYK and FLT3 inhibition profile, and encouraging single agent response rate in relapsed/refractory AML, we are also interested in exploring its activity in biomarker-defined subsets of AML where SYK inhibition has been shown to be particularly effective.

Mivavotinib has the potential to be the first treatment specifically for non-GCB (ABC) DLBCL, a population of patients with a historically poorer prognosis and therefore high unmet need, and potential to be the first treatment for a genetically-defined subset of ABC in patients with MyD88/CD79 mutations. An oral drug with enriched efficacy in a subset of DLBCL with high unmet need would address an important therapeutic gap in the current treatment landscape.

mTORC1/2 Inhibitor Sapanisertib (CB-228)

A total of 50,000-60,000 sqNSCLC patients are diagnosed in the United States each year, comprising 25-30% of all NSCLC. Only 1-5% of squamous NSCLC tumors have actionable mutations, such as EGFR, KRAS, etc. The five-year metastatic survival rate among sqNSCLC patients is 7%. Standard-of-care for 1L therapy consists of an anti-PD-1 agent and chemotherapy. For 2L therapy,

standard of care is salvage chemotherapy, which is associated with a median progression-free survival, or PFS, of 3 to 4.5 months. NRF2 (also known as NFE2L2) mutations occur in approximately 15% of patients, and KEAP mutations occur in approximately 12% of patients with sqNSCLC. Patients with tumors harboring the NRF2 or KEAP1 mutation are known to have significantly poorer outcomes compared to wild-type NRF2/KEAP1 tumors. Therefore, NRF2 mutated sqNSCLC represents an especially high unmet need subpopulation of lung cancer for which there are currently no effective therapies.

Sapanisertib is a potent and selective, dual mTORC1/2 inhibitor that targets a key survival mechanism in KEAP1/NRF2-mutated tumor cells. Activating mutations in NRF2 or inactivating mutations in KEAP1 lead to constitutive activation of the oxidative stress pathway, enhancing tumor growth and survival. NRF2 activation has been shown to upregulate the mTOR pathway. In preclinical studies evaluating the anti-tumor activity of sapanisertib across a panel of NSCLC cell lines, the most potent antitumor activity was seen in NRF2 mutant sqNSCLC, while it was not active in NRF2 wild-type cell lines. Additionally, it showed moderate activity in KEAP1 mutant cell lines and was inactive in KEAP1 WT cells. In a preclinical study where a panel of mTORC inhibitors were tested on a NRF2 mutated sqNSCLC mouse xenograft model, only sapanisertib showed strong single agent efficacy, while TORC1 inhibitors everolimus and deferolimus were inactive, supporting the need for dual TORC1/2 inhibition in NRF2 mutated sqNSCLC.

In a recent Phase 2 trial, sapanisertib demonstrated durable single agent activity with 27% (or 3/11) confirmed ORR in a subset of heavily pretreated NRF2-mutated sqNSCLC patients. In comparison, ORR was 17% (or 1/6) in KEAP1-mutated sqNSCLC and 0% (or 0/5) in patients with KEAP1-mutated/KRAS-mutated adenocarcinoma subtype of NSCLC. Responses in NRF2-mutated sqNSCLC patients were durable, and the NRF2-mutant cohort had a median PFS of 8.9 months (95% CI: 7 months, not reached). Historic standard of care treatment with salvage chemotherapy has a median PFS of 3 to 4.5 months. These promising data and high unmet need led us to design a two-part phase 2 study of relapsed/refractory sqNSCLC patients with or without NRF2-mutations as detected by next generation sequencing, or NGS.

Sapanisertib has a well-established and manageable safety profile. In three separate trials in patients with NSCLC and other R/R solid tumors, sapanisertib at 3-5mg QD was well tolerated, with treatment-emergent adverse events, or TEAE, being predominantly Grade 1/2. The most commonly observed TEAE was hyperglycemia, which was well controlled with oral hypoglycemic therapy and home glucose monitoring. Out of 93 patients treated across these five studies, only one patient discontinued for hyperglycemia at evaluated QD doses. The most common Grade ³3 TEAE was hyperglycemia at 25% (or 23/93), followed by rash macular and fatigue at 8% each, and hypophosphatemia, abdominal pain, and hyponatremia at 4% each.

We are initiating a two-part Phase 2 study of sapanisertib monotherapy in NRF2-mutated sqNSCLC patients. The phase 2a part of the study will evaluate sapanisertib 2 mg BID or 3 mg QD in patients with sqNSCLC harboring either WT or mutated NRF2, as detected by NGS. The objectives of phase 2a are dose refinement and confirmation of the selective activity in NRF2-mutated tumors compared to WT tumors to validate NRF2 mutation as the selection biomarker. Enrollment is expected to begin in the second quarter of 2022. Data generated from this study could position the company to initiate a registrational study in NRF2-mutated squamous NSCLC. The phase 2b part of the study, which could be registration enabling, will be informed by data from phase 2a, and is planned to be a single-arm expansion study evaluating sapanisertib in NRF2-mutated sqNSCLC patients at the selected dose targeting accelerated approval, and/or a randomized study comparing sapanisertib versus standard of care.

Subsequent development in sqNSCLC could involve monotherapy and/or combinations with standard of care therapies in earlier lines of therapy within the biomarker-defined populations. NRF2- and KEAP1-mutations have been detected across several tumor types at frequencies up to 27%, providing additional indications for development of sapanisertib as a monotherapy and in combination beyond sqNSCLC.

Sapanisertib has the potential to be a first-in-class treatment for NRF2-mutated sqNSCLC patients, a patient population with poorer prognosis, high unmet need, and no targeted therapies, as well as a possible treatment for other NRF2-mutated cancers beyond NSCLC.

Synthetic Lethality Preclinical Pipeline

We continue to leverage our discovery engine to build a preclinical pipeline of synthetic lethality targets with a focus on paralog genes. In June 2021, we became a member of the Broad Institute of MIT and Harvard's, or the Broad Institute's, Cancer Dependency Map, or DepMap, Consortium. The goal of the DepMap initiative at the Broad Institute is to discover new targets and biomarkers for precision cancer medicines. Membership in the DepMap Consortium is an opportunity for us to generate novel data for discovery programs and forge deeper collaborations with the Broad Institute’s data and computational scientists in order to enable translational decisions for our programs. We plan to utilize this partnership with the Broad Institute to continue to explore biomarkers for our clinical programs, as well as identify biomarker-defined subpopulations of cancer patients for undisclosed pipeline programs.

VPS4A Inhibitors

We presented data describing novel VPS4A inhibitors discovered by Calithera at the American Association for Cancer Research, or AACR, 2022 Annual Meeting. The presented poster detailed Calithera's discovery of a novel series of VPS4A inhibitors that are currently advancing through lead optimization. These data validate the synthetic lethal interaction between the gene paralogs vacuolar protein sorting-associated protein 4A (VPS4A) and 4B (VPS4B), and provide the first preclinical evidence supporting a newly discovered series of compounds designed to target these proteins for cancer treatment.

We mined CRISPR genetic loss-of-function data and associated molecular datasets from the DepMap project datasets to identify pairs of gene paralogs, which were then prioritized for potential drug targets. This work resulted in the identification of VPS4A and VPS4B as promising targets. We then conducted multiple studies to validate the paralog gene pair, demonstrating that cells with VPS4B homozygous or heterozygous loss are sensitive to VPS4A knock down while cells without VPS4B loss are not. In addition, simultaneously knocking down VPS4A and VPS4B consistently resulted in cell death.

Utilizing the VPS4A and VPS4B paralog genes as targets, we identified a novel series of small molecule inhibitors. Among the findings shared at AACR are data detailing the performance of one inhibitor of VPS4A and VPS4B ATPase activity, compared to notably inactive previously reported VPS4 inhibitors. To our knowledge, our internally-discovered VPS4 inhibitors are the first active, on-target inhibitors of VPS4. Potent, selective, and pharmacologically active VPS4 inhibitors are expected to be well-tolerated and have strong single-agent activity in tumors with these mutations. We are currently advancing multiple inhibitors in the series through lead optimization.

Additional Small Molecule Programs

IL4I1 Inhibitor CB-668

We have also discovered CB-668, a first-in-class, potent, orally administered inhibitor of the immune-suppressive enzyme IL4I1. IL4I1 is an enzyme that is expressed by tumor cells and antigen presenting cells that metabolizes phenylalanine, tyrosine and tryptophan to produce hydrogen peroxide, an inhibitor of T-cell function. In particular, IL4I1 can metabolize tryptophan to kynurenic acid and other metabolites that lead to immunosuppression in the tumor microenvironment. Preclinical data were presented at the 2020 Society for Immunotherapy of Cancer (SITC) Annual Meeting. In syngeneic mouse models CB-668 exhibited immune mediated, single agent activity and augmented activity in combination with checkpoint inhibitors. IL4I1 expression has been correlated with poor clinical outcomes and expression is elevated in multiple tumor types including ovarian and B-cell tumors.

Arginase Inhibitor for Cystic Fibrosis (CB-280)

Our product candidate, CB-280 is a novel oral inhibitor of arginase being evaluated for the treatment of cystic fibrosis, or CF. In 2020, we were awarded up to $2.4 million from the Cystic Fibrosis Foundation to support development of CB-280. In 2021 we presented interim data from the Phase 1b trial at the North American Cystic Fibrosis Conference (NACFC) for cohorts 1-3. CB-280 was well tolerated, demonstrated linear pharmacokinetics (PK), and showed complete and continuous target inhibition in plasma at doses at or above 100mg. CB-280 also demonstrated robust pharmacodynamic (PD) effects, with rapid and significant dose-proportional increases in plasma arginine, the key driver of NO production. The study is now complete. We plan on publishing the Ph1b data in the future. We are not pursuing further development of CB-280 in CF at this time, due to recent significant shifts in the CF therapeutic and regulatory landscape.

Glutaminase Inhibitor telaglenastat (CB-839)

In November 2021, we announced the discontinuation of the phase 2 telaglenastat KEAPSAKE clinical trial in patients with non-squamous NSCLC with genetic mutations in KEAP1/NRF2 based on a lack of clinical benefit observed in patients treated with telaglenastat in an interim analysis. The phase 2 randomized, placebo-controlled, double-blind KEAPSAKE study was designed to evaluate the safety and anti-tumor activity of telaglenastat plus standard-of-care chemoimmunotherapy as front-line therapy among patients with stage IV non-squamous non-small cell lung cancer (NSCLC) whose tumors have a KEAP1 or NRF2 mutation. At the time of unblinding on October 27, 2021, there were 40 patients randomized. The available efficacy data at unblinding, including investigator-assessed progression-free survival (PFS), did not demonstrate clinical benefit, and analysis of the data led to the conclusion that there was a very low probability for the study to achieve a positive result. No difference in safety profile was seen between the two arms.

Partnered Programs

Arginase Inhibitor for Oncology (INCB001158)

An additional arginase inhibitor, INCB001158, was discovered by Calithera and is being developed by Incyte Corporation, or Incyte, for oncology and hematology indications, and is currently being evaluated in Phase 1/2 trials in combination with other anti-cancer agents.

CD73 Inhibitor (CB-708; ATG037) for Oncology

A highly potent, selective, orally-bioavailable small molecule inhibitor of CD73, CB-708 (now ATG037) was discovered by Calithera. Preclinical data were presented at the AACR 2019 Annual Meeting and the 2019 SITC meeting demonstrating that CB-708 has immune-mediated, single agent activity in syngeneic mouse tumor models. In May 2021, we entered into a license agreement with Antengene Investment Limited, or Antengene, a wholly-owned subsidiary of Antengene Corporation, where we granted Antengene an exclusive, worldwide license to develop and commercialize CB-708 (now ATG-037). In February 2022, Antengene announced the approval of a first-in-human study of ATG-037 in patients with locally advanced or metastatic solid tumors.

Critical Accounting Policies and Estimates

There have been no significant changes in our critical accounting policies and estimates disclosed in our Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the SEC.

Financial Overview

Our Ability to Continue as a Going Concern

We had cash and cash equivalents of approximately $44.7 million as of March 31, 2022. On April 1, 2022, we received $8.5 million in net proceeds after underwriting discounts, commissions and offering costs from our public offering. In accordance with Accounting Standards Codification, or ASC, 205-40, *Going Concern*, we evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern within one year after the date that the condensed consolidated financial statements are issued on May 10, 2022. This evaluation initially does not take into consideration the potential mitigating effect of our plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists under this methodology, we evaluate whether the mitigating effect of our plans sufficiently alleviate substantial doubt about our ability to continue as a going concern. The mitigating effect of our plans, however, is only considered if both (1) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued, and (2) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about our ability to continue as a going concern within one year after the date that the financial statements are issued. In performing this analysis, we excluded certain elements of our operating plan that cannot be considered probable. Under ASC 205-40, the future receipt of potential funding from future sales of shares of our capital stock, if received, cannot be considered probable at this time because none of the plans are entirely within our control and have not been approved by our board of directors as of the date of the financial statements. Therefore, our expectation to generate operating losses and negative operating cash flows in the future and our need for additional funding to support our planned operations raise substantial doubt regarding our ability to continue as a going concern for a period of one year after the date that these financial statements are issued.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of the uncertainties described above.

Research and Development Expenses

Research and development expenses represent costs incurred to conduct research, such as the discovery and development of our product candidates. We recognize all research and development costs as they are incurred. Costs associated with co-development activities performed under our collaboration agreements and award are included in research and development expenses, with any reimbursement of costs reflected as a reduction of such expenses.

Research and development expenses consist primarily of the following:

- employee-related expenses, which include salaries, benefits and stock-based compensation;
- expenses incurred under agreements with clinical trial sites that conduct research and development activities on our behalf;

- laboratory and vendor expenses related to the execution of preclinical studies and clinical trials;
- contract manufacturing expenses, primarily for the production of clinical supplies;
- facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation expense and other supplies;
- license fees and milestone payments related to our licensing agreements; and
- the asset acquisition of sapanisertib and mivavotinib.

The largest component of our total operating expenses has historically been our investment in research and development activities including the clinical development of our product candidates. We allocate to research and development expenses the salaries, benefits, stock-based compensation expense, and indirect costs of our clinical and preclinical programs on a program-specific basis, and we include these costs in the program-specific expenses.

The following table shows our research and development expenses for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,	
	2022	2021
	(in thousands)	
Development candidate:		
Sapanisertib (CB-228)	$ 2,301	$ —
Mivavotinib (CB-659)	1,981	—
Telaglenastat (CB-839)	2,259	11,705
CB-280	847	1,779
Total development	7,388	13,484
Preclinical and research:		
Preclinical and research	2,178	1,855
Total	$ 9,566	$ 15,339

We expect our research and development expenses will increase during the next few years as we advance our product candidates into and through clinical trials, and pursue regulatory approval of our product candidates. The process of conducting clinical trials necessary to obtain regulatory approval is costly and time consuming. We may never succeed in achieving marketing approval for our product candidates. The probability of success of our product candidates may be affected by numerous factors, including clinical data, competition, manufacturing capability and commercial viability. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist of personnel costs, allocated expenses and other expenses for outside professional services, including legal, audit and accounting services, insurance, investor relations and other expenses associated with being a public company. Personnel costs consist of salaries, benefits and stock-based compensation. Allocated expenses consist of facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation expense and other supplies. We have incurred and expect to continue to incur additional expenses as a result of operating as a public company, including costs to comply with the rules and regulations applicable to companies listed on a national securities exchange, costs related to compliance and reporting obligations pursuant to the rules and regulations of the SEC and other governing bodies and, potentially, the costs related to increases in our administrative functions to support the growth of our business as we advance our product candidates.

Results of Operations

Comparison of the Three Months Ended March 31, 2022 and 2021

	Three Months Ended March 31,		Change	
	2022	2021	$	%
	(in thousands, except percentages)			
Operating expenses:				
Research and development	$ 9,566	$ 15,339	$ (5,773)	-38%
General and administrative	4,260	5,428	(1,168)	-22%
Total operating expenses	13,826	20,767	(6,941)	-33%
Loss from operations	(13,826)	(20,767)	6,941	-33%
Interest and other income (expense), net	(9)	372	(381)	-102%
Net loss	$ (13,835)	$ (20,395)	$ 6,560	-32%

Research and Development. Research and development expenses decreased $5.8 million, or 38%, from $15.3 million for the three months ended March 31, 2021 to $9.6 million for the three months ended March 31, 2022. The decrease of $5.8 million was due to a $9.5 million decrease in the telaglenastat program and a $0.9 million decrease in the CB-280 program, partially offset by a $2.3 million increase due to the sapanisertib program, a $2.0 million increase due to the mivavotinib program, and a $0.3 million increase in our early stage research.

General and Administrative. General and administrative expenses decreased $1.2 million, or 22%, from $5.4 million for the three months ended March 31, 2021, to $4.3 million for the three months ended March 31, 2022. The decrease of $1.2 million was due to a $1.1 million decrease in personnel-related costs, primarily from decreases in stock-based compensation expense, salaries and severance, and a $0.1 million decrease in professional services costs.

Interest and Other Income (Expense), net. Interest and other income (expense), net decreased $0.4 million, or 102%, from $0.4 million for the three months ended March 31, 2021 to ($9,000) for the three months ended March 31, 2022. The decrease of $0.4 million related to a gain on the remeasurement of our lease liability during the three months ended March 31, 2021.

Liquidity and Capital Resources

As of March 31, 2022, we had cash and cash equivalents totaling $44.7 million. Our operations have been financed by net proceeds from the sale of shares of our capital stock and payments from our collaboration and licensing agreements.

Public Offering

On April 1, 2022, we closed an underwritten public offering of 18,518,519 shares of our common stock at a combined price to the public of $0.54 per share and accompanying common warrants for gross proceeds to us of $10 million, and net proceeds of $8.5 million after underwriting discounts, commissions and offering costs. Each share of common stock is accompanied by a warrant to purchase one share of common stock at an exercise price of $0.54 per share, which is immediately exercisable and will expire 18 months from the date of issuance, or a short-term warrant, and a warrant to purchase one share of common stock at an exercise price of $0.54 per share, which is immediately exercisable and will expire 5 years from the date of issuance, or a long-term warrant.

Millennium Asset Purchase Agreement

On October 18, 2021, we entered into an Asset Purchase Agreement, or APA, with Millennium. In accordance with the APA, we entered into a Preferred Stock Purchase Agreement pursuant to which we agreed to issue to Millennium 1,000,000 shares of our Series A convertible preferred stock, or the Series A preferred stock. The Series A preferred stock is initially convertible at the option of the holder into approximately 17.2 shares of common stock, based on our $2.04 per share closing stock price from October 15, 2021. The conversion rate of the Series A preferred stock is subject to anti-dilution adjustments that if triggered would result in the issuance of additional shares of common stock upon conversion. We intend to seek stockholder approval at our next regular stockholder meeting for the issuance of the shares of common stock above 20% in accordance with the rules of The Nasdaq Stock Market LLC, including additional shares that may become issuable as a result of any price-based anti-dilution adjustments. The Series A preferred stock has the preferences, rights and limitations set forth in the Certificate of Designations, as filed with the Secretary of State of the State of Delaware. If we are unable to obtain stockholder approval in accordance with the rules of The Nasdaq Stock Market LLC for the conversion of all of the shares of Series A preferred stock to common stock, and as a result Millennium is unable to convert any portion of the Series A preferred stock to common stock, then we and Millennium will negotiate in good faith the timing and amount per share to be paid to compensate Millennium for such inability to convert. If we are able to obtain stockholder approval in accordance with the rules of The Nasdaq Stock Market LLC for the conversion of all of the shares of Series A preferred stock to common stock but Millennium is unable to convert as a result of the Accounting Cap (defined as 19.99% of the outstanding common stock of the Company on any date) any portion of the Series A preferred stock to common stock by the five year anniversary of the issue date, then on each yearly anniversary thereafter, any shares of Series A preferred stock that remain outstanding shall automatically be converted into common stock at the applicable conversion ratio, in each case subject to the Accounting Cap, until such point in time as all shares of Series A preferred stock have been converted.

Shelf Registration Statement

In August 2020, we filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission, or SEC, which permits the offering, issuance and sale by us of up to a maximum aggregate offering price of $250 million of our common stock. As of March 31, 2022, $227.9 million of our common stock remained available for sale, of which $62.9 million may be issued and sold pursuant to an "at-the-market" offering program, or ATM program, for sales of our common stock under a sales agreement with Jefferies LLC, subject to certain conditions as specified in the sales agreement. Our ability to sell securities under the shelf registration statement and the ATM program will be limited until we are no longer subject to the SEC's "baby shelf" limitations.

Our primary uses of cash are to fund operating expenses, primarily research and development expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Our expectation to generate operating losses and negative operating cash flows in the future and the need for additional funding to support our planned operations raise substantial doubt regarding our ability to continue as a going concern for a period of one year after the date that these condensed consolidated financial statements are issued on May 10, 2022. We believe that our existing cash and cash equivalents as of May 10, 2022, will be sufficient for us to meet our current operating plan through the second quarter of 2023. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially based on a number of factors including the extent and magnitude of the impact from the COVID-19 pandemic, in particular the challenges associated with opening new and enrolling existing clinical studies. Based on current planning assumptions, we intend to announce data from our sapanisertib and mivavotinib Phase 2 studies by the first quarter of 2023. If data from these trials are not available until after the end of the second quarter of 2023, we will require additional capital to release these data. In addition, in order to complete the process of obtaining regulatory approval for our product candidates and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our product candidates, if approved, we will require substantial additional funding.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the timing and costs of our planned clinical trials for our product candidates;
- the timing and costs of our planned preclinical studies of our product candidates;
- our success in establishing and scaling commercial manufacturing capabilities;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- subject to receipt of regulatory approval, revenue received from commercial sales of our product candidates;
- the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make in connection with the licensing, filing, prosecution, maintenance, defense and enforcement of any patents or patent applications or other intellectual property rights; and
- the extent to which we in-license or acquire other products and technologies.

We plan to continue to fund our operations and capital funding needs through equity and/or debt financing. We may also consider further collaborations or selectively partnering for clinical development and commercialization. The sale of additional equity would result in additional dilution to our stockholders. The incurrence of debt financing would result in debt service obligations and the instruments governing such debt could provide for operating and financing covenants that would restrict our operations. If we are not able to secure adequate additional funding we may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, and/or suspend or curtail planned programs. The continued spread of COVID-19 and uncertain market conditions may limit our ability to access capital. Any of these actions could harm our business, results of operations and future prospects.

Cash Flows

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

	Three Months Ended March 31,	
	2022	2021
	(in thousands)	
Cash used in operating activities	$ (16,010)	$ (22,002)
Cash provided by investing activities	$ —	$ 6,500
Cash provided by financing activities	$ 1,137	$ 9,537

Cash used in operating activities was $16.0 million for the three months ended March 31, 2022, compared to $22.0 million for the three months ended March 31, 2021. The decrease of $6.0 million in cash used in operating activities mainly related to decreased research and development costs, primarily in our telaglenastat program.

Cash provided by investing activities was zero and $6.5 million for the three months ended March 31, 2022 and 2021, respectively, and for the three months ended March 31, 2021 was related to proceeds from the sale and maturity of investments.

Cash provided by financing activities was $1.1 million and $9.5 million for the three months ended March 31, 2022 and 2021, respectively. For the three months ended March 31, 2022 and 2021, we received $1.1 million and $9.5 million, respectively, in net proceeds from the sale and issuance of common stock related to our at-the-market offering program.

Contractual Obligations and Other Commitments

There have been no material changes to the contractual obligations during the three months ended March 31, 2022, as compared to those disclosed in our Annual Report on Form 10-K for the year ended December 31, 2021.

Recent Accounting Pronouncements

Please refer to Note 2 to our unaudited condensed consolidated financial statements appearing under Part I, Item 1 for a discussion of recent accounting pronouncements.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

During the three months ended March 31, 2022, there were no material changes to our market risk disclosures as set forth in Part II, Item 7A, “Quantitative and Qualitative Disclosures About Market Risk” in our Annual Report on Form 10-K for the year ended December 31, 2021.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures.

As of March 31, 2022, management, with the participation of our Chief Executive Officer and Chief Financial Officer, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission’s rules and forms, and that such information is accumulated and communicated to our management, including the Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding required disclosures.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and our Chief Financial Officer concluded that, as of March 31, 2022, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control Over Financial Reporting.

There were no changes in our internal control over financial reporting during the three months ended March 31, 2022, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. – OTHER INFORMATION

Item 1. Legal Proceedings

From time to time, we may become involved in legal proceedings relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations, financial condition or cash flows.

Item 1A. Risk Factors

Risk Factors

Our business involves significant risks, some of which are described below. You should carefully consider the following risk factors, in addition to the other information contained in the reports we file with the Securities and Exchange Commission, or the SEC. The occurrence of any of the events or developments described in the following risk factors could harm our business, financial condition, results of operations, cash flows, the trading price of our common stock and our growth prospects. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Current Report on Form 10-Q. The risks relating to our business set forth in our Annual Report on Form 10-K, filed with the SEC, are set forth below and are unchanged substantively as of the date of this filing, except for those risks designated by an asterisk (*).

Summary Risk Factors

Our business is subject to numerous risks and uncertainties, including those highlighted in the section titled “Risk Factors” immediately following this summary. These risks include, among others, the following:

- We have incurred significant operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or maintain profitability.
- There is substantial doubt regarding our ability to continue as a going concern. We will need substantial additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.
- Our business, operations and clinical development plans and timelines are currently adversely affected by and could be adversely affected in the future by the effects of health epidemics, including the recent COVID-19 pandemic, on the manufacturing, clinical trial and other business activities performed by us or by third parties with whom we conduct business, including our contract manufacturers, Clinical Research Organizations, or CROs, shippers and others.
- Our approach to the discovery and development of product candidates that target tumor metabolism and tumor immunology is unproven and may never lead to marketable products.
- Our drug discovery and development efforts might not generate successful product candidates.
- We may not realize the anticipated benefits from our acquisition of the Takeda assets.
- If it is determined that companion diagnostics are needed for the Takeda Programs, we may be unable to successfully develop companion diagnostics for biomarkers that enable patient selection, or experience significant delays in doing so, we may not realize the full commercial potential of the Takeda Programs.
- If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive 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.
- If we experience delays or difficulties in enrolling patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.
- If serious adverse effects or unexpected characteristics of our product candidates are identified during development, we may need to abandon or limit our development of some or all of our product candidates.
- Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- Product liability lawsuits against us could cause us to incur substantial liabilities and could limit the commercialization of any product candidates we may develop.

- If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.
- We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing and manufacture our product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.
- Our arginase inhibitors program in hematology and oncology indications, including INCB001158, is reliant in part on Incyte for the successful development and commercialization in a timely manner. If Incyte does not devote sufficient resources to INCB001158's development, is unsuccessful in its efforts, or chooses to terminate its agreement with us, our business, operating results and financial condition will be harmed.
- We have in the past and may seek in the future to selectively establish collaborations, and, if we are unable to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.
- Our internal computer systems, or those used by our Clinical Research Organizations or other contractors or consultants, may fail or suffer security breaches.
- If we are alleged to infringe intellectual property rights of third parties, our business could be harmed.
- We may not be able to protect, or fully exploit, our intellectual property rights throughout the world, which could impair our competitive position.
- Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be impaired.
- 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.
- Our future success depends on our ability to retain our senior management team and to attract, retain and motivate qualified personnel.
- The holders of our Series A preferred stock have liquidation and other rights that are senior to the rights of the holders of shares of our common stock.
- We may be required to issue a significant number of additional shares of common stock for no additional consideration to the holders of our Series A preferred stock pursuant to certain price-based anti-dilution provisions.
- We cannot take certain actions without the consent of a majority of the holders of the Series A preferred stock.
- We may be required to make significant cash payments to the holders of Series A preferred stock if we do not receive requisite stockholder approval to allow the conversion of the Series A preferred stock to common stock.
- We have granted Millennium registration rights with respect to the shares of common stock into which our Series A preferred stock is convertible. If these additional shares are sold, or it is perceived that they will be sold, the market price of our common stock could decline.
- The trading price of our common stock is likely to be volatile, and purchasers of our common stock could incur substantial losses.
- Concentration of ownership of our capital stock may prevent new investors from influencing significant corporate decisions.
- If we are unable to maintain proper and effective internal controls over financial reporting, the accuracy and timeliness of our financial reporting and the market price of our common stock may be adversely affected.
- If we are unable to adequately address these and other risks we face, our business, financial condition, operating results and prospects may be adversely affected.
- The price of our common stock and our stockholders' (deficit) equity does not meet the requirements for continued listing on the Nasdaq Global Select Market. If we fail to maintain or regain compliance with the minimum listing requirements, our common stock will be subject to delisting. Our ability to publicly or privately sell equity securities and the liquidity of our common stock could be adversely affected if our common stock is delisted.

Risk Factors

Risks Related to Our Financial Position and Need For Additional Capital

We have incurred significant operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or maintain profitability.*

- Since our inception, we have incurred significant operating losses. Our net loss was $13.8 million for the three months ended March 31, 2022 and $115.1 million for the year ended December 31, 2021, respectively. As of March 31, 2022, we had an accumulated deficit of $505.2 million. To date, we have financed our operations through sales of our capital stock and payments from the Incyte Collaboration Agreement. We have devoted substantially all of our financial resources and efforts to research and development. We expect that it may be many years, if ever, before we receive regulatory approval and have a product candidate ready for commercialization. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if and as we:
- advance further into clinical trials for our existing clinical product candidates, sapanisertib, mivavotinib and CB-280;
- continue the preclinical development of our research programs and advance candidates into clinical trials;
- identify additional product candidates and advance them into preclinical development;
- pursue regulatory approval of product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we obtain marketing approval;
- become obligated to make milestone payments pursuant to the APA;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, commercial, regulatory and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support product development and commercialization;
- acquire or in-license other product candidates and technologies; and
- operate as a public company.

We have never generated any revenue from product sales and may never be profitable. To become and remain profitable, we and/or our collaborators must develop and eventually commercialize one or more products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those product candidates for which we may obtain marketing approval, and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenue that is significant or large enough to achieve profitability. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

There is substantial doubt regarding our ability to continue as a going concern. We will need substantial additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.*

As of March 31, 2022, our cash and cash equivalents were $44.7 million. On April 1, 2022, we received net proceeds of $8.5 million related to our public offering after underwriting discounts, commissions and offering costs. Based on our current business plan, there is substantial doubt regarding our ability to continue as a going concern for a period of one year after the date that our financial statements for the quarter ended March 31, 2022 are issued. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, continue and initiate clinical trials of, potentially prepare for commercial launch of, and seek marketing approval for our product candidates, specifically sapanisertib, mivavotinib, and CB-280, and as we become obligated to make milestone payments pursuant to our outstanding license and asset purchase agreements. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution of the approved product.

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

- the scope, progress, results and costs of drug discovery, clinical development, laboratory testing and clinical trials for our product candidates, in particular sapanisertib, mivavotinib and CB-280;
- the costs, timing and outcome of any regulatory review of our product candidates, sapanisertib, mivavotinib and CB-280;
- the cost of any other product programs we pursue;
- the costs and timing of commercialization activities, including manufacturing, marketing, sales and distribution, for any product candidates that receive, or that we anticipate may receive, marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- milestone payments pursuant to our outstanding license and asset purchase agreements;
- achieving the total remaining potential development, regulatory and commercialization milestones set forth in the Incyte Collaboration Agreement;
- our obligations to redeem shares of Series A preferred stock;
- our ability to establish and maintain collaborations on favorable terms, if at all; and
- the extent to which we acquire or in-license other product candidates and technologies.

Identifying potential product candidates and conducting preclinical studies and clinical trials are time consuming, expensive and uncertain processes that take years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales for any of our current or future product candidates. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenue, if any, will be derived from sales of products that may not be commercially available for many years, if at all.

We do not have any material committed external source of funds or other support for our development efforts other than the Incyte Collaboration Agreement for the development and commercialization of small molecule arginase inhibitors in hematology and oncology indications, including INCB001158, which agreement is terminable by Incyte for convenience or following our uncured breach. If the Incyte Collaboration Agreement is terminated, we would need to obtain substantial additional sources of funding to develop INCB001158 as currently contemplated. If such additional funding is not available on favorable terms or at all, we may need to delay or reduce the scope of our INCB001158 development program or dedicate resources allocated to other programs to fund INCB001158. We may also need to grant rights in the United States, as well as outside the United States, to INCB001158 to one or more partners.

Accordingly, we will need substantial additional funding in connection with our continuing operations and to achieve our goals. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional financing due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our operating plans.

Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to further revise our business plan and strategy, which may result in us significantly curtailing, delaying or discontinuing one or more of our research or development programs or may result in our being unable to expand our operations or otherwise capitalize on our business opportunities. As a result, our business, financial condition and results of operations could be materially affected.

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 revenue, we expect to finance our cash needs through a combination of equity and debt financings, as well as entering into new collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds, other than our collaborations, which are limited in scope and duration. To the

extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, and may be secured by all or a portion of our assets. If we raise funds by entering into new collaborations, strategic alliances or licensing arrangements in the future with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or through collaborations, strategic alliances or licensing arrangements 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.

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

We were founded in March 2010 and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and commencing Phase 1 and 2 clinical trials of our product candidates. CB-280, sapanisertib, mivavotinib are currently being or will be evaluated by us in Phase 1 and Phase 2 clinical trials, respectively. All of our other programs are in research and preclinical development. We have not yet demonstrated our ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials required for regulatory approval of our product candidates, obtain marketing 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 commercialization. Typically, it takes many years to develop one new product from the time it is discovered to when it is commercially available. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history or if we had product candidates in advanced clinical trials.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors that may alter or delay our plans. If a product candidate is approved, we will need to transition from a company with a research and development focus to a company capable of supporting successful commercial activities. We may not be successful in any step in such a transition.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Sections 382 and 383 place a limitation on the amount of taxable income which can be offset by carryforward tax attributes, such as net operating losses or tax credits, after a change in control. Generally, after a change in control, a loss corporation cannot deduct carryforward tax attributes in excess of the limitation prescribed by Section 382 and 383. Therefore, certain of our carryforward tax attributes may be subject to an annual limitation regarding their utilization against taxable income in future periods. As a result of our IPO in 2014, we triggered an "ownership change" as defined in Internal Revenue Code Section 382 and related provisions. Additionally, due to stock acquired by investors and reported under Section 13(g), we believe that an “ownership change” occurred during 2018, as well. Subsequent ownership changes since 2018 may subject us to annual limitations of our net operating loss and credit carryforwards. Such annual limitation could result in the expiration of the net operating loss and credit carryforwards before utilization.

Furthermore, our ability to use our net operating losses and other tax attributes to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income before the expiration dates of the net operating losses, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use all of our net operating losses. Federal net operating losses generated prior to 2018 will continue to be governed by the net operating loss tax rules as they existed prior to the adoption of the Tax Cuts and Jobs Act of 2017, or Tax Act, which means that generally they will expire 20 years after they were generated if not used prior thereto. Under the Tax Act, as modified by the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, signed into law on March 27, 2020, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses will be limited to 80% of current year taxable income.

Our effective tax rate may fluctuate, and tax authorities may disagree with our positions and conclusions regarding certain tax positions, resulting in unanticipated costs, taxes or non-realization of expected benefits.

Our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the newly enacted federal income tax law, changes in the mix of our profitability between jurisdictions in which we are or may become subject to tax, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable nexus, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

Risks Related to Drug Discovery, Development and Commercialization

Our business, operations and clinical development plans and timelines are currently adversely affected by and could be adversely affected in the future by the effects of health epidemics, including the recent COVID-19 pandemic, on the manufacturing, clinical trial and other business activities performed by us or by third parties with whom we conduct business, including our contract manufacturers, Clinical Research Organizations, or CROs, shippers and others.

Our business could be adversely affected in the future by health epidemics wherever we have clinical trial sites or other business operations. In addition, health epidemics could cause significant disruption in the operations of third-party manufacturers, CROs and other third parties upon whom we rely. For example, in December 2019, a novel strain of coronavirus, SARS-CoV-2, causing a disease referred to as COVID-19, was reported to have surfaced in Wuhan, China. Since then, COVID-19 has spread to multiple countries worldwide, including the United States. In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic, and the U.S. government imposed travel restrictions on travel between the United States, Europe and certain other countries. Further, the President of the United States declared the COVID-19 pandemic a national emergency and invoked powers under the Stafford Act, the legislation that directs federal emergency disaster response, and under the Defense Production Act, the legislation that facilitates the production of goods and services necessary for national security and for other purposes. Similarly, the State of California declared a state of emergency related to the spread of COVID-19, and the Governor of California and other health officials in California have announced aggressive orders, health directives and recommendations to reduce the spread of the disease. On March 16, 2020, the Health Officer of San Mateo County, the county in which our headquarters is located, issued a "Shelter in Place" Order requiring, among other things, the closure of all non-essential businesses. Further, the Governor of California issued an executive order directing that all non-essential businesses close their physical operations and implement work-from-home schedules, effective as of March 19, 2020. We have implemented work-from-home policies for all employees. The effects of the executive order and our work-from-home policies may continue to negatively impact productivity, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. For example, the CANTATA trial was fully enrolled in October 2019, and we previously advised that we planned to report top-line efficacy and safety data from the trial in the late third quarter or fourth quarter of 2020. In light of delays associated with COVID-19, top-line data was announced in early first quarter 2021. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results and financial condition.

We depend on a worldwide supply chain to manufacture products used in our preclinical studies and clinical trials. Quarantines, shelter-in-place and similar government orders, or the expectation that such orders, shutdowns or other restrictions could occur, whether related to COVID-19 or other infectious diseases, could impact personnel at third-party manufacturing facilities in the United States and other countries, or the availability or cost of materials, which could disrupt our supply chain.

If our relationships with our suppliers or other vendors are terminated or scaled back as a result of the COVID-19 pandemic or other health epidemics, we may not be able to enter into arrangements with alternative suppliers or vendors or do so on commercially reasonable terms or in a timely manner. Switching or adding additional suppliers or vendors involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new supplier or vendor commences work. As a result, delays may occur, which could adversely impact our ability to meet our desired clinical development and any future commercialization timelines. Although we carefully manage our relationships with our suppliers and vendors, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not harm our business.

In addition, our preclinical studies and clinical trials have been and may continue to be affected by the COVID-19 pandemic. Clinical site initiation, patient enrollment and activities that require visits to clinical sites, including data monitoring, have been and may continue to be delayed due to prioritization of hospital resources toward the COVID-19 pandemic or concerns among patients about participating in clinical trials during a pandemic. Some patients may have difficulty following certain aspects of clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Similarly, if we are unable to successfully recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 or experience additional restrictions by their institutions, city, or state our clinical trial operations could be adversely impacted.

The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a widespread pandemic could result

in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The global pandemic of COVID-19 continues to evolve rapidly. The ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations, and we continue to monitor the COVID-19 situation closely.

We may not realize the anticipated benefits from our acquisition of the Takeda assets.

In October 2021, we acquired and licensed from Millennium certain technology, intellectual property and other assets related to the Takeda Programs, including certain patents and know-how solely related to the Takeda Programs and necessary for the exploitation of products containing the CB-228 and CB-659 compounds, as well as specified regulatory materials, agreements, materials and inventory related to the Takeda Programs. This transaction may require us to incur non-recurring and other charges, increase our near and long-term expenditures, impair relationships with key suppliers, upstream licensors or other licensees, pose significant integration challenges, require additional expertise, result in dilution to our existing stakeholders and disrupt our management and business, which could harm our operations and financial results. Under the agreement with Millennium, we are required to pursue commercially reasonable efforts to develop, and subsequently to commercialize, at least one CB-228 product and one CB-659 product in each of the United States, Japan and certain European countries. If we fail to properly exercise such efforts to develop and commercialize the Takeda Programs as specified in the asset purchase agreement, or otherwise breach the asset purchase agreement, we may be subject to various claims by Millennium and parties affiliated with Millennium, including claims that could result in the termination of the asset purchase agreement and the licenses and other rights granted to us thereunder. In addition, the development of the Takeda Programs and the other products and technologies acquired or licensed may not be successful or they may require significantly greater resources and investments than originally anticipated. Conversely, the liabilities assumed in the transaction could be greater than originally anticipated. As a result, the anticipated benefits of the acquisition may not be realized fully within the expected timeframe or at all or may take longer to realize or cost more than expected, which could harm our business, financial condition, results of operations and growth prospects.

Further, while we seek to mitigate risks and liabilities of the acquisition and in-licensing transaction, and other potential acquisitions and in-licensing transactions, through, among other things, due diligence, there may be risks and liabilities that such due diligence efforts fail to discover, that are not disclosed to us, or that we inadequately assess. If we breach, or have assumed liability for a breach of, any license agreement or other contract assigned to us pursuant to the asset purchase agreement, including a breach of the diligence or payment obligations under such contracts, we may be subject to various claims by the counterparties to such contracts, including claims that could result in the termination of such contracts or the loss of the licenses and other rights granted to us thereunder. Any failure in identifying and managing these risks, liabilities and uncertainties effectively, could harm our business, results of operations and financial condition.

If it is determined that companion diagnostics are needed for the Takeda Programs, we may be unable to successfully develop companion diagnostics for biomarkers that enable patient selection, or experience significant delays in doing so, we may not realize the full commercial potential of the Takeda Programs.

If not already commercially available, we may be required to seek collaborations with diagnostic companies for the development of diagnostics for biomarkers associated with the Takeda Programs. We may have difficulty in establishing or maintaining such development relationships, and we will face competition from other companies in establishing these collaborations. Furthermore, even if a diagnostic is commercially available, we may not be able to obtain reimbursement for its use without obtaining regulatory approval.

The development of companion diagnostic products requires a significant investment of working capital, and may not result in any future income. This could require us to raise additional funds, which could dilute our current investors or impact our ability to continue our operations in the future.

There are also risks associated with diagnostics that are commercially available, including that we may not have access to reliable supply for such diagnostics. Market acceptance of the companion diagnostic may be low as a result of the cost and complexity of utilizing such companion diagnostic. Furthermore, if commercial tumor profiling panels are not able to be updated to include additional tumor-associated genes, or if clinical oncologists do not incorporate molecular or genetic sequencing into their clinical practice, we may not be successful in developing or commercializing the Takeda Programs.

We may attempt to secure approval from the FDA through the use of accelerated approval pathways for the Takeda Programs. If we are unable to obtain such approval, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.

We may in the future seek accelerated approval for our one or more of our product candidates, including the Takeda Programs. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verity and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug. In addition, the FDA currently requires pre-approval of promotional materials for accelerated approval products, once approved.

If we decide to submit an application for accelerated approval for our product candidates, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA could require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidates would result in a longer time period to commercialization of such product candidate, if any, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Our approach to the discovery and development of product candidates that target tumor metabolism and tumor immunology is unproven and may never lead to marketable products.

Our scientific approach focuses on using our understanding of cellular metabolic pathways and the role of glutaminase in these pathways, as well as the role of arginase in the anti-tumor immune response, to identify molecules that are potentially promising as therapies for cancer indications. Any product candidates we develop may not effectively modulate metabolic or immunology pathways. The scientific evidence to support the feasibility of developing product candidates based on inhibiting tumor metabolism or impacting the anti-tumor immune response are both preliminary and limited. Although preclinical studies suggest that inhibiting glutaminase can suppress the growth of certain cancer cells, to date no company has translated this mechanism into a drug that has received marketing approval. Even if we are able to develop a product candidate in preclinical studies, we may not succeed in demonstrating the safety and efficacy of the product candidate in human clinical trials. Our expertise in cellular metabolic pathways, the role of glutaminase in these pathways, and the role of arginase in the anti-tumor immune response may not result in the discovery and development of commercially viable products to treat cancer.

Our drug discovery and development efforts might not generate successful product candidates.

We have invested a significant portion of our efforts and financial resources in the identification or asset acquisition of our most advanced product candidates, sapanisertib, mivavotinib, INCB001158 and CB-280, which are being or will be evaluated in Phase 1 and Phase 2 clinical trials. We have entered into the Incyte Collaboration Agreement for the development and commercialization of INCB001158. Pursuant to the agreement, we and Incyte collaborated on the development of the licensed products for hematology and oncology indications, including INCB001158. Effective September 30, 2020, we have opted out of our co-development obligations and as a result, Incyte will solely develop INCB001158 or any other licensed products. All of our other programs are in research and preclinical development. INCB001158 will be developed for use in combination with other approved therapies, and as such, we will be dependent upon the continued marketing availability of the drugs that are used in combination with them. As a result, the timing and costs of the regulatory paths we will follow and marketing approvals remain uncertain. Our ability to generate product revenue, which may not occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of sapanisertib, mivavotinib, INCB001158 and CB-280. The success of sapanisertib, mivavotinib, INCB001158, CB-280 and any other product candidates we may develop will depend on many factors, including the following:

- successful enrollment in, and completion of, clinical trials;
- demonstrating safety and efficacy;
- receipt of marketing approvals from applicable regulatory authorities;

- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our product candidates;
- developing a sales and marketing organization or outsourcing these functions to third parties;
- launching commercial sales of the product candidates, if and when approved, whether alone or selectively in collaboration with others;
- developing and commercializing sapanisertib, mivavotinib and small molecule arginase inhibitors, including INCB001158;
- acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- a continued acceptable safety profile of the products following approval;
- enforcing and defending intellectual property rights and claims; and
- other legal, regulatory, compliance, privacy, and fraud and abuse matters.

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

We may not be successful in our efforts to identify or discover potential product candidates for clinical development.

Our drug discovery efforts may not be successful in identifying compounds that are useful in treating cancer. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons. In particular, our research methodology used may not be successful in identifying compounds with sufficient potency or bioavailability to be potential product candidates. In addition, our potential product candidates may, on further study, be shown to have harmful side effects or other negative characteristics. Research programs to identify new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on potential product candidates that ultimately prove to be unsuccessful. If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to generate product revenue, which would harm our financial position and adversely impact our stock price.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive 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.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials could occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a particular clinical trial do not necessarily predict final results of that trial. For example, our CANTATA trial of telaglenastat in RCC did not meet the primary endpoint of PFS despite earlier encouraging results in this indication in a Phase 1b trial.

Moreover, preclinical and clinical data are often susceptible to multiple interpretations and analyses. 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.

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

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- 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;

- 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;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate; and
- 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.
- 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 that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

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

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the U.S. Food and Drug Administration, or the FDA, or analogous regulatory authorities outside the United States. In addition, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- availability and efficacy of approved medications for the disease under investigation;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of health care professionals;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. 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 effects or unexpected characteristics of our product candidates are identified during development, we may need to abandon or limit our development of some or all of our product candidates.

We or our collaborators are currently evaluating or plan to evaluate sapanisertib, mivavotinib, INCB001158 and CB-280 in Phase 1 and Phase 2 clinical trials. All our other programs are in research and preclinical development and their risk of failure 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 marketing approval. Adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, any current or future collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label, or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If adverse effects were to arise in patients being treated with any of our product candidates, it could require us to halt, delay or interrupt clinical trials of such product candidate or adversely affect our ability to obtain requisite approvals to advance the development and commercialization of such product candidate. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many agents that initially showed promise in early stage testing for treating cancer or other diseases have later been found to cause side effects that prevented further development of the agent.

We are in early clinical trials and we have seen several adverse events, or AEs, deemed possibly or probably related to study drug in each of those programs. For example, in our evaluation of telaglenastat with nivolumab, during the dose escalation of the combination therapy, there was one report of dose limiting Grade 3 ALT increase. We have treated an insufficient number of patients to fully assess the safety of telaglenastat and INCB001158 and, as these trials progress, we may experience frequent or severe adverse events. Our ongoing and planned trials for sapanisertib, mivavotinib and CB-280 and Incyte's ongoing and planned trials for INCB001158 may fail due to safety issues, and we may need to abandon development of product candidates from these programs. Our other research programs may fail due to preclinical or clinical safety issues, causing us to abandon or delay the development of a product candidate from these programs.

Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may experience delays in designing and executing clinical trials to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or our current and future collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

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.

We have limited financial and managerial resources. 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, including our agreement with Incyte, in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. In addition, under our agreement with Incyte, Incyte has the right to commercialize INCB001158 in hematology and oncology indications. If Incyte does not successfully commercialize INCB001158, we may be unable to realize the full value from our collaboration with Incyte.

Even if any of our product candidates receives marketing approval, we or others may later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any future collaborators, to market the product.

Clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, 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, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or any future collaborators, may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by health care professionals, patients, third party payors and others in the medical community necessary for commercial success.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by health care professionals, patients, third party payors and others in the medical community for us to achieve commercial success. For example, current cancer treatments like chemotherapy and radiation therapy for certain diseases and conditions are well established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue to 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 compared to alternative treatments;
- our ability to offer any approved products for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of health care professionals to prescribe these therapies;
- the strength of marketing and distribution support;
- third-party coverage and sufficient reimbursement; and
- the prevalence and severity of any side effects.

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

We do not have a sales and marketing infrastructure to support any future commercialization efforts. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a robust sales and marketing organization and/or outsource these functions to other third parties. For our small molecule arginase inhibitors in hematology and oncology indications, including INCB001158, we will be dependent on Incyte’s sales and marketing infrastructure to effectively commercialize these products. In the future, we may choose to build a focused sales and marketing infrastructure to sell some of our product candidates, if and when they are approved, excluding INCB001158.

There are risks involved both with establishing our own sales and marketing capabilities and with entering into arrangements with third parties to perform these services. 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. This 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 product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to health care professionals or persuade adequate numbers of health care professionals to prescribe any future products; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability of these product revenue to us may be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing 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. Research and discoveries by others may result in breakthroughs which may render our products obsolete even before they generate any revenue. 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 the cancer indications for which we are focusing our product development efforts. 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.

We are developing our product candidates for the treatment of various cancers. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well-established therapies and are widely accepted by health care professionals, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic products. This may make it difficult for us to achieve our business strategy of using our product candidates in combination with existing therapies or replacing existing therapies with our product candidates.

Our primary competitors or product candidates in clinical development in either NRF2-mutated cancers, or with similar mechanism to an mTORC1/2 inhibitor are Antengene Corporation, Celcuity, Inc. Our primary competitors or product candidates in clinical development for biomarker-defined diffuse large B-cell lymphoma or with a similar mechanism to a SYK inhibitor are Alexion Pharmaceuticals, Inc., Curis, Inc., Genentech, Inc., HutchMed (China) Limited, Karyopharm Therapeutics, MorphoSys AG. Our primary competitors in the field of Cystic Fibrosis include AbbVie, Inc., Beyond Air Inc., Corbus Pharmaceuticals Holdings, Inc., Novartis AG, Novoteris, LLC, Proteostatis Therapeutics, Inc., Translate Bio, Inc., and Vertex Pharmaceuticals, Inc.

Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. In addition, our competitors may discover biomarkers that more efficiently measure metabolic pathways than our methods, which may give them a competitive advantage in developing potential products. Our competitors may also obtain marketing approval from the FDA or other regulatory authorities for their products sooner 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. Many of our competitors 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

may 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.

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

The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. In the United States, new 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 marketing approval is granted. As a result, we might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay its commercial launch, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the drug in that country. Adverse pricing limitations may hinder our ability to commercialize and generate revenue from one or more product candidates, even if our product candidates obtain marketing approval.

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 programs, 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 significant 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 payment 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 may not be available for any product that we commercialize and, if coverage is available, the level of reimbursement may not be sufficient. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for coverage does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Coverage and reimbursement rates may vary according to the use of the drug and the medical circumstances under which it is used, may be based on reimbursement levels already set for lower cost products or procedures or 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 policies and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded programs 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 our approved products and our overall financial condition.

In addition, there has been heightened governmental scrutiny of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. We expect additional healthcare reform initiatives to be adopted in the future, particularly in light of the new presidential administration. We continue to monitor and evaluate the potential impact of these legislative actions and their effect on our business and operations.

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop after approval. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates 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; and
- the inability to commercialize any products we may develop.

Although we maintain product liability insurance coverage in the amount of up to $10.0 million per claim and in the aggregate, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage as we continue clinical trials and if we successfully commercialize any products. 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 we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive 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. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees in our workplace, including those 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, chemical, 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. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing and manufacture our product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We currently rely and expect to continue to rely on third parties, such as our collaborators, contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials and to conduct some aspects of our research and preclinical testing. Any of these third parties may terminate their engagements with us at any time. 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 commercialize our product candidates. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If we need to enter into alternative arrangements, it would delay our product development activities.
Our reliance on these third parties for research and development activities, including our reliance on Millennium and Takeda for prior preclinical and clinical research and development activities relating to the Takeda Programs, will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial, and that all clinical trial activities conducted by our contract research organizations follow applicable laws and regulations, and are conducted in an ethical and compliant manner. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government sponsored database, available at www.clinicaltrials.gov, within certain timeframes. Failure by us, or any of the third parties working on our behalf, to do the above can result in fines, adverse publicity and civil and criminal sanctions.

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third party manufacturers for the manufacture of our product candidates for preclinical studies and clinical trials and for commercial supply of any of these product candidates for which we obtain marketing approval. To date, we have obtained or plan to obtain materials for sapanisertib,

mivavotinib, INCB001158 and CB-280 for our current and planned clinical trials from third-party manufacturers. We have engaged third party manufacturers to obtain the active ingredient for INCB001158 and CB-280 for pre-clinical testing and clinical trials. We do not have a long-term supply agreement with any third-party manufacturers, and we purchase our required drug supply on a purchase order basis.

We may be unable to establish agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

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

Third-party manufacturers may not be able to comply with current U.S. Good Manufacturing Practice requirements, or cGMPs, or similar legal and regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates, operating restrictions and criminal prosecutions, any of which could adversely affect supplies of our product candidates and harm our business and results of operations.

Any product that we may develop may compete with other product candidates and products for access to these manufacturing facilities. There are a limited number of manufacturers that operate under cGMPs 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 for bulk drug substances. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there 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 product candidates that receive marketing approval on a timely and competitive basis.

We also currently rely, and expect to continue to rely, on third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of these third parties could delay clinical development or marketing approval of our product candidates or commercialization of our drugs, producing additional losses and depriving us of potential revenue. Although we believe that there are several potential alternative third parties who could store and distribute drug supplies for our clinical trials, we may incur added costs and delays in identifying and qualifying any such replacement.

Our arginase inhibitors program in hematology and oncology indications, including INCB001158, is reliant in part on Incyte for the successful development and commercialization in a timely manner. If Incyte does not devote sufficient resources to INCB001158's development, is unsuccessful in its efforts, or chooses to terminate its agreement with us, our business, operating results and financial condition will be harmed.

In January 2017, we and Incyte Corporation entered into the Incyte Collaboration Agreement. Pursuant to the Incyte Collaboration Agreement, we granted Incyte an exclusive, worldwide license to develop and commercialize small molecule arginase inhibitors, including INCB001158, for hematology and oncology indications. We retained rights to certain arginase inhibitors that are not part of the collaboration for specific orphan indications outside of hematology and oncology, including cystic fibrosis. Pursuant to the Incyte Collaboration Agreement, we and Incyte collaborated on, and co-funded the development of, the licensed products for hematology and oncology indications, including INCB001158, with Incyte bearing 70% and Calithera bearing 30% of global development costs. Effective September 30, 2020, we opted out of our co-development obligations and as a result, Incyte will pay all costs and solely develop INCB001158 or any other licensed products.

The Incyte collaboration may not be clinically or commercially successful due to a number of important factors, including the following:

- Subject to the terms of our collaboration agreement, including diligence obligations, although Incyte has certain obligations to use commercially reasonable efforts to develop and commercialize INCB001158, Incyte has discretion in determining the efforts and resources that it will apply to its partnership with us. The timing and amount of any development milestones, and downstream commercial milestones and royalties that we may receive under such

partnership will depend on, among other things, the efforts, allocation of resources and successful development and commercialization of INCB001158;

- Incyte may select a dose for INCB001158 that does not have a favorable benefit/risk profile;
- Incyte may terminate its partnership with us without cause and for circumstances outside of our control, which could make it difficult for us to attract new strategic partners or adversely affect how we are perceived in scientific and financial communities; and
- Incyte may develop or commercialize INCB001158 in a way that exposes us to potential litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability.

In April 2020, we filed a complaint against Incyte in Superior Court of California, San Francisco County, asserting claims for breach of contract arising out of Incyte's failure to pay two milestone payments we believe are due under the Incyte Collaboration Agreement. On September 14, 2021, we entered into a Settlement Agreement and Release with Incyte, or the Settlement Agreement. Pursuant to the Settlement Agreement, which resolves all claims in the complaint without any admission of liability or fault, Incyte will pay us a negotiated settlement amount and the parties have exchanged mutual releases. Concurrently, the parties also filed a dismissal of the action in the Superior Court of California.

If we were to terminate our agreement with Incyte due to Incyte's breach, or if Incyte were to terminate the agreement without cause, there could be a delay in the return of our rights to INCB001158 and the development and commercialization of INCB001158 would be delayed, curtailed or terminated because we may not have sufficient financial resources or capabilities to continue development and commercialization on our own.

Incyte may enter into one or more transactions with third parties, including a merger, consolidation, reorganization, sale of substantial assets, sale of substantial stock or other change in control, which could divert the attention of its management and adversely affect Incyte's ability to retain and motivate key personnel who are important to the continued development of the small molecule arginase inhibitor program. In addition, the third party to any such transaction could reprioritize Incyte's development programs which could delay the development of our programs or cause Incyte to terminate the agreement.

We have in the past and may seek in the future to selectively establish collaborations, and, if we are unable to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. In addition to our collaboration with Incyte, for some of our product candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We may also be restricted under existing license agreements from engaging in research and development activities or entering into future agreements on certain terms with potential collaborators. For example, pursuant to our license agreement with Symbioscience, we have agreed not to develop any other arginase inhibitors for use in human healthcare outside of the scope of that agreement. In addition, under our agreement with Incyte, we are not allowed to develop any retained arginase inhibitors (small molecule arginase inhibitors, other than INCB001158, retained by us for research and development in non-hematology/oncology indications) for any indication except specific orphan indications outside of hematology and oncology.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, 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 for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate.

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

If we decide to collaborate with any other third parties in connection with any of our development programs or product candidates, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so,

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

To the extent we enter into any other collaborations, we may depend on such collaborations for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of our product candidates.

We may selectively seek additional third-party collaborators for the development and commercialization of our product candidates. Our current and any future collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. Pursuant to these arrangements and any potential future arrangements, we will 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 revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. Collaborations involving our product candidates, including our collaboration with Incyte, pose many risks to us, including that:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- Collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates 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;
- Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates or products if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- A collaborator with marketing and distribution rights to one or more product candidates or products may not commit sufficient resources to the marketing and distribution of such drugs;
- Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- Disputes may arise between the collaborators and us, for example our prior claims against Incyte, that result in the delay or termination of the research, development or commercialization of our product candidates or products, or that result in costly litigation or arbitration that diverts management attention and resources;
- We may lose certain valuable rights under circumstances identified in our collaborations if we undergo a change of control;
- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and
- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.
- We have in-licensed a portfolio of arginase inhibitors as part of our efforts to develop product candidates for the arginase program, and we are substantially dependent on this in-license for that program. We have acquired sapanisertib and mivavotinib from Millennium. As part of that acquisition from Millennium, Millennium assigned to us certain patents and know-how solely related to sapanisertib and mivavotinib. Millennium also granted us a license under certain other intellectual property necessary for the exploitation of such products. To the extent any such licenses are terminated, our business may be harmed.

Our internal computer systems, or those used by our Clinical Research Organizations or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems, and those of our Clinical Research Organizations and other third parties on which we rely, are vulnerable to damage from computer viruses and unauthorized access, malware, natural disasters, fire, terrorism, war and telecommunication, electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. While we have not experienced any such material system failure or security breach to our knowledge to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our future product candidates could be delayed.

Risks Related to Our Intellectual Property

Recent laws and rulings by U.S. courts make it difficult to predict how patents will be issued or enforced in our industry.

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. There have been numerous recent changes to the patent laws and to the rules of the United States Patent and Trademark Office, or the USPTO, which may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the Leahy-Smith America Invents Act, which was signed into law in 2011, includes a transition from a "first-to-invent" system to a "first-to-file" system, and changes the way issued patents are challenged. Certain changes, such as the institution of *inter partes* review proceedings, came into effect on September 16, 2012. Substantive changes to patent law associated with the America Invents Act may affect our ability to obtain patents, and, if obtained, to enforce or defend them in litigation or post-grant proceedings, all of which could harm our business.

Furthermore, the patent positions of companies engaged in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Two cases involving diagnostic method claims and "gene patents" have recently been decided by the Supreme Court. On March 20, 2012, the Supreme Court issued a decision in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, or *Prometheus*, a case involving patent claims directed to measuring a metabolic product in a patient to optimize a drug dosage amount for the patient. According to the Supreme Court, the addition of well-understood, routine or conventional activity such as "administering" or "determining" steps was not enough to transform an otherwise patent ineligible natural phenomenon into patent eligible subject matter. On July 3, 2012, the USPTO issued guidance indicating that process claims directed to a law of nature, a natural phenomenon or an abstract idea that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied and the claim amounts to significantly more than the natural principle itself should be rejected as directed to non-statutory subject matter. On June 13, 2013, the Supreme Court issued its decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, or *Myriad*, a case involving patent claims held by Myriad Genetics, Inc. relating to the breast cancer susceptibility genes BRCA1 and BRCA2. *Myriad* held that isolated segments of naturally occurring DNA, such as the DNA constituting the BRCA1 and BRCA2 genes, is not patent eligible subject matter, but that complementary DNA, which is an artificial construct that may be created from RNA transcripts of genes, may be patent eligible.

We cannot assure you that our efforts to seek patent protection for our technology and products will not be negatively impacted by the decisions described above, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact the Supreme Court's decisions in *Prometheus* and *Myriad* may have on the ability of life science companies to obtain or enforce patents relating to their products and technologies in the future.

Moreover, although the Supreme Court has held in *Myriad* that isolated segments of naturally occurring DNA are not patent-eligible subject matter, certain third parties could allege that activities that we may undertake infringe other gene-related patent claims, and we may deem it necessary to defend ourselves against these claims by asserting non-infringement and/or invalidity positions, or pay to obtain a license to these claims. In any of the foregoing or in other situations involving third-party intellectual property rights, if we are unsuccessful in defending against claims of patent infringement, we could be forced to pay damages or be subjected to an injunction that would prevent us from utilizing the patented subject matter. Such outcomes could harm our business.

If we are alleged to infringe intellectual property rights of third parties, our business could be harmed.

Our research, development and commercialization activities may be alleged to infringe patents, trademarks or other intellectual property rights owned by other parties. Certain of our competitors and other companies in the industry have substantial patent portfolios and may attempt to use patent litigation as a means to obtain a competitive advantage. We may be a target for such litigation. Even if our pending patent applications issue, they may relate to our competitors' activities and may therefore not deter litigation against us. The risks of being involved in such litigation may also increase as we become more visible as a public company and move into new markets and applications for our product candidates. There may also be patents and patent applications that are relevant to our technologies or product candidates that are unknown to us. For example, certain relevant patent applications may have been filed but not published. If such patents exist, or if a patent issues on any of such patent applications, that patent could be asserted against us. Third parties could bring claims against us that would cause us to incur substantial expenses and, if the claims against us are successful, could cause us to pay substantial damages, including treble damages and attorneys' fees for willful infringement. The defense of such a suit could also divert the attention of our management and technical personnel. Further, if an intellectual property infringement suit were brought against us, we could be forced to stop or delay research, development or sales of the product that is the subject of the suit.

As a result of infringement claims, or to avoid potential claims, we may choose or be compelled to seek intellectual property licenses from third parties. These licenses may not be available on acceptable terms, or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us likely would be nonexclusive, which would mean that our competitors also could obtain licenses to the same intellectual property. Ultimately, we could be prevented from commercializing a product candidate and/or technology or be forced to cease some aspect of our business operations if, as a result of actual or threatened infringement claims, we are unable to enter into licenses of the relevant intellectual property on acceptable terms. Further, if we attempt to modify a product candidate and/or technology or to develop alternative methods or products in response to infringement claims or to avoid potential claims, we could incur substantial costs, encounter delays in product introductions or interruptions in sales.

We may become involved in other lawsuits to protect or enforce our patents or other intellectual property, which could be expensive and time-consuming, and an unfavorable outcome could harm our business.

In addition to the possibility of litigation relating to infringement claims asserted against us, we may become a party to other patent litigation and other proceedings, including *inter partes* review proceedings, post-grant review proceedings, derivation proceedings declared by the USPTO and similar proceedings in foreign countries, regarding intellectual property rights with respect to our current or future technologies or product candidates or products. The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could impair our ability to compete in the marketplace.

Competitors may infringe or otherwise violate our intellectual property, including patents that may issue to or be licensed by us. As a result, we may be required to file claims in an effort to stop third-party infringement or unauthorized use. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. This can be expensive, particularly for a company of our size, and time-consuming, and even if we are successful, any award of monetary damages or other remedy we may receive may not be commercially valuable. In addition, in an infringement proceeding, a court may decide that our asserted intellectual property is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our intellectual property does not cover its technology. An adverse determination in any litigation or defense proceedings could put our intellectual property at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

If the breadth or strength of our patent or other intellectual property rights is compromised or threatened, it could allow third parties to commercialize our technology or products or result in our inability to commercialize our technology and products without infringing third-party intellectual property rights. Further, third parties may be dissuaded from collaborating with us.

Interference or derivation proceedings brought by the USPTO or its foreign counterparts may be necessary to determine the priority of inventions with respect to our patent applications, and we may also become involved in other proceedings, such as re-examination proceedings, before the USPTO or its foreign counterparts. Due to the substantial competition in the pharmaceutical space, the number of such proceedings may increase. This could delay the prosecution of our pending patent applications or impact the validity and enforceability of any future patents that we may obtain. In addition, any such litigation, submission or proceeding may be resolved adversely to us and, even if successful, may result in substantial costs and distraction to our management.

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. Moreover, intellectual property law relating to the fields in which we operate is still evolving and, consequently, patent and other intellectual property positions in our industry are subject to change and are often uncertain. We may not prevail in any of these suits or other efforts to protect our technology, and the damages or other remedies awarded, if any, may not be commercially valuable. During the course of this type of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

We may not be able to protect, or fully exploit, our intellectual property rights throughout the world, which could impair our competitive position.

Filing, prosecuting, defending and enforcing patents on all of our technologies, product candidates and products throughout the world would be prohibitively expensive. As a result, we seek to protect our proprietary position by filing patent applications in the United States and in select foreign jurisdictions and cannot guarantee that we will obtain the patent protection necessary to protect our competitive position in all major markets. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export infringing products to territories where we may obtain patent protection but where enforcement is not as strong as that in the United States. These products may compete with our current and future products in jurisdictions where we do not have any issued patents, and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or the marketing of competing products in violation of our proprietary rights generally. The legal systems of certain countries make it difficult or impossible to obtain patent protection for pharmaceutical products and services. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and could divert our efforts and attention from other aspects of our business.

Even if we do secure patents in foreign jurisdictions, the legal systems in certain of those countries might require us, as examples, to do business through an entity that is partially owned by a local investor, or to grant license rights to local partners in a manner not required by the jurisdictions in which we currently operate. Requirements such as the foregoing could limit our ability to fully exploit and in the future monetize our product candidates and patents, as well as placing potential additional difficulties on our enforcement efforts in those jurisdictions.

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

In addition to seeking patents for some of our technologies and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention assignment agreements with our employees and consultants that obligate them to assign to us any inventions developed in the course of their work for us. However, we cannot guarantee that we have executed these agreements with each party that may have or have had access to our trade secrets or that the agreements we have executed will provide adequate protection. 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. As a result, we may be forced to bring claims against third parties, or defend claims that they bring against us, to determine ownership of what we regard as our intellectual property. Monitoring unauthorized disclosure is difficult and we do not know whether the procedures we have followed to prevent such disclosure have been or will be adequate. 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 the United States may be less willing or unwilling to protect trade secrets. If any of the technology or information that we protect as trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them 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, our competitive position would be harmed.

If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest, and our business may be harmed.

Our trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be infringing on other marks. As a means to enforce our trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings. This can be expensive and time-consuming, particularly for a company of our size. In addition, in an infringement proceeding, a court may decide that a trademark of ours is not valid or is

unenforceable, or may refuse to stop the other party from using the trademark at issue. We may not be able to protect our rights to these and other trademarks and trade names which we need to build name recognition by potential partners or customers in our markets of interest. We do not currently have any registered trademarks in the United States. Any trademark applications in the United States and in other foreign jurisdictions where we may file may not be allowed or may subsequently be opposed. In addition, other companies in the biopharmaceutical space may be using trademarks that are similar to ours and may in the future allege that our use of the trademark infringes or otherwise violates their trademarks. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be harmed.

Third parties may assert ownership or commercial rights to inventions we develop.

Third parties may in the future make claims challenging the inventorship or ownership of our intellectual property. We have written agreements with collaborators that provide for the ownership of intellectual property arising from our collaborations. In some instances, there may not be adequate written provisions to address clearly the resolution of intellectual property rights that may arise from a collaboration. If we cannot successfully negotiate sufficient ownership and commercial rights to the inventions that result from our collaborations, or if disputes otherwise arise with respect to the intellectual property developed in the course of a collaboration, we may be limited in our ability to capitalize on the market potential of these inventions.

In addition, we may face claims by third parties that our agreements with employees, contractors or consultants obligating them to assign intellectual property to us are ineffective or are in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and interfere with our ability to capture the commercial value of such inventions. Litigation may be necessary to resolve an ownership dispute, and if we are not successful, we may be precluded from using certain intellectual property, or may lose our exclusive rights in that intellectual property. Either outcome could have an adverse impact on our business.

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 may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. 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.

The process of obtaining marketing approvals, both in the United States and elsewhere, is expensive, may take many years and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. We cannot assure you that we will ever obtain any marketing approvals in any jurisdiction. 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. The FDA and comparable authorities in other countries 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 or other studies, and clinical trials. In addition, varying interpretations of the data obtained from preclinical testing and clinical trials could delay, limit or prevent marketing approval of a product candidate. Additionally, 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.

Any product candidate for which we obtain marketing approval could be subject to marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products.

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. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements, quality assurance and corresponding maintenance of records and documents and requirements regarding the distribution of samples to health care professionals and recordkeeping. 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, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine. The FDA closely regulates the post approval marketing and promotion of drugs to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. Companies may only share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling.

In addition, later discovery of previously unknown problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling, marketing, distribution or use of a product;
- requirements to conduct post-approval clinical trials;
- warning 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 revenue;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

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

Healthcare providers, customers and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare providers, customers 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 research, as well as market, sell and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- the federal false claims laws, including the False Claims Act, which can be enforced through civil whistleblower or qui tam actions, impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for, among other things, executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, on certain covered healthcare providers, health plans, and healthcare clearinghouses and their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information as well as their covered subcontractors with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies to report to the Centers for Medicare & Medicaid Services, or CMS, an agency within the Department of Health and Human Services, or HHS, information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report information regarding payments and other transfers of value provided during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiologist assistants, and certified nurse midwives during the previous year; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers, marketing expenditures and/or drug pricing, and other state and local laws require the registration of pharmaceutical sales representatives.

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 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, possible exclusion from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, imprisonment, integrity oversight and reporting obligations to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations. If any of the health care professionals or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.*

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.

Additionally, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the PPACA, enacted in 2010, made a number of substantial changes in the way healthcare is financed by both governmental and private insurers. There have been executive, judicial, and Congressional challenges to certain aspects of the PPACA. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under PPACA have been signed into law. The Tax Act included a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the PPACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the PPACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the PPACA marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the PPACA. It is possible that the PPACA will be subject to judicial or Congressional challenges in the future. It is unclear how such

challenges and the healthcare reform measures of the Biden administration will impact the PPACA. We continue to evaluate the potential impact of PPACA and its possible repeal or replacement on our business.

Policy changes, including potential modification or repeal of all or parts of the PPACA or the implementation of new health care legislation could result in significant changes to the health care system, which may prevent us from being able to generate revenue, attain profitability or commercialize our drugs. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand or lower pricing for our product candidates, or additional pricing pressures.

Further, there has been heightened governmental scrutiny of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule on September 24, 2020, effective November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2023. On November 20, 2020, CMS issued an interim final rule implementing the Trump administration's Most Favored Nation, or MFN, executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. As a result of litigation challenging the MFN model, on August 10, 2021, CMS published a proposed rule that seeks to rescind the MFN Model interim final rule. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy", with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. In addition, Congress is considering drug pricing as part of the budget reconciliation process.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which includes reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute will remain in effect through 2030 unless additional Congressional action is taken. However, COVID-19 relief legislation suspended the 2% Medicare sequester from May 1, 2020 through the end of March 2022. From April 2022 through June 2022, a 1% sequester cut will be in effect, with the full 2% cut resuming thereafter. It is possible that additional governmental action will be taken in response to the COVID-19 pandemic. We expect that healthcare reform measures may be adopted in the future, particularly in light of the new presidential administration, which could have a material adverse effect on our industry generally and on our ability to maintain or increase sales of any of our product candidates that we successfully commercialize.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our senior management team and to attract, retain and motivate qualified personnel.

We are highly dependent upon our senior management team, as well as the other principal members of our research and development teams. All of our executive officers are employed "at will," meaning we or they may terminate the employment relationship at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these 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. 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. 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.

We may need to expand our operations, and may encounter difficulties in managing our growth, which could disrupt our business.

In the future, we may need to expand the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. To manage our future growth, we may need to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. We may not be able to effectively manage an expansion of our operations or recruit and train additional qualified personnel. Moreover, an expansion of our operations may lead to significant costs and may divert our management and business development resources. For example, our facilities expenses may increase, or decrease, which will vary depending on the time and terms of any facility lease or sublease we may enter into from time to time. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

We may engage in acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. Because we have not made any acquisitions to date, our ability to do so successfully is unproven. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may fail to strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

International expansion of our business exposes us to business, regulatory, political, operational, financial and economic risks associated with doing business in various jurisdictions globally.

Our business strategy incorporates international expansion, including establishing and maintaining relationships with service providers, distributors and manufacturers globally. Doing business internationally involves a number of risks, including:

- multiple, conflicting and changing laws and regulations such as tax laws, export and import restrictions, employment laws, anti-bribery and anti-corruption laws, regulatory requirements and other governmental approvals, permits and licenses;
- failure by us or our distributors to obtain appropriate licenses or regulatory approvals for the sale or use of our product candidates, if approved, in various countries;
- difficulties in managing foreign operations;
- complexities of foreign reimbursement regimes and price controls;
- financial risks, such as difficulty enforcing contracts exposure to foreign currency exchange rate fluctuations;
- reduced protection for intellectual property rights;
- reduced protection of contractual rights in the event of bankruptcy or insolvency of the other contracting party;
- natural disasters, political and economic instability, including wars, terrorism and political unrest, outbreak of disease, boycotts, curtailment of trade and other business restrictions;
- difficulties in complying with changes in laws, regulations and costs affecting our foreign operations, including our United Kingdom, or UK, operations potentially affected by the UK exiting the European Union, or EU;
- failure to comply with foreign laws, regulations, standards and regulatory guidance governing the collection, use, disclosure, retention, security and transfer of personal data, including the European Union General Data Privacy

Regulation, or GDPR, which introduces strict requirements for processing personal data of individuals within the European Union; and

- failure to comply with the United Kingdom Bribery Act 2010, or UK Bribery Act, and similar antibribery and anticorruption laws in other jurisdictions, and the Foreign Corrupt Practices Act, including its books and records provisions and its anti-bribery provisions, including by failing to maintain accurate information and control over sales and distributors' activities.

The UK's withdrawal from the EU, commonly referred to as Brexit, may have a negative effect on global economic conditions, financial markets and our business.

Following the result of a referendum in 2016, the United Kingdom left the European Union on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom was subject to the Transition Period through December 31, 2020 during which European Union rules continued to apply. Negotiations between the United Kingdom and the European Union are expected to continue in relation to the customs and trading relationship between the United Kingdom and the European Union following the expiry of the Transition Period.

The lack of clarity over which EU laws and regulations will continue to be implemented in the United Kingdom after the Transition Period (including financial laws and regulations, tax and free trade agreements, intellectual property rights, data protection laws, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws) may negatively impact foreign direct investment in the United Kingdom, increase costs, depress economic activity and restrict access to capital. The uncertainty concerning the United Kingdom's legal, political and economic relationship with the European Union after the Transition Period may be a source of instability in the international markets, create significant currency fluctuations, and/or otherwise adversely affect trading agreements or similar cross-border co-operation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise).

These developments, or the perception that any of them could occur, have had, and may continue to have, a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and limit the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the United Kingdom's financial and banking markets, as well as on the regulatory process in Europe. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility.

If the United Kingdom and the European Union are unable to negotiate acceptable withdrawal terms or if other EU Member States pursue withdrawal, barrier-free access between the United Kingdom and other EU Member States or among the European Economic Area, or EEA, overall could be diminished or eliminated. The long-term effects of Brexit will depend on any agreements (or lack thereof) between the United Kingdom and the European Union and, in particular, any arrangements for the United Kingdom to retain access to EU markets after the Transition Period.

Such a withdrawal from the European Union is unprecedented, and it is unclear how the United Kingdom's access to the European single market for goods, capital, services and labor within the European Union, or single market, and the wider commercial, legal and regulatory environment, will impact us.

Risks Related to Our Securities

The price of our common stock currently does not meet the requirements for continued listing on the Nasdaq Global Select Market. If we fail to maintain or regain compliance with the minimum listing requirements, our common stock will be subject to delisting. Our ability to publicly or privately sell equity securities and the liquidity of our common stock could be adversely affected if our common stock is delisted.*

The continued listing standards of the Nasdaq Global Select Market, or Nasdaq, require, among other things, that the minimum price of a listed company's stock be at or above $1.00. If the minimum bid price is below $1.00 for a period of more than 30 consecutive trading days, the listed company will fail to be in compliance with Nasdaq's listing rules and, if it does not regain compliance within the grace period, will be subject to delisting. The bid price of our common stock closed below the minimum $1.00 per share requirement and on December 30, 2021 we received a notification of noncompliance from Nasdaq. In accordance with Nasdaq's listing rules, we have been afforded 180 calendar days to regain compliance with the bid price requirement. In order to regain compliance, the bid price of our common stock must close at a price of at least $1.00 per share for a minimum of 10 consecutive trading days.

In addition, on April 7, 2022, we received a written notice, or the Notice, from the Listing Qualifications Staff of The Nasdaq Stock Market LLC notifying us that our stockholders' equity as reported in our Annual Report on Form 10-K for the year ended

December 31, 2021, did not satisfy the continued listing requirement under Nasdaq Listing Rule 5450(b)(1)(A) for the Nasdaq Global Select Market, which requires that a listed company's stockholders' equity be at least $10.0 million. In accordance with such Notice, we have 45 calendar days from the date of the Notice to submit a plan to regain compliance with Nasdaq Listing Rule 5450(b)(1)(A), or we may choose to transfer the listing of our common stock to The Nasdaq Capital Market. We intend to submit a compliance plan within 45 days of the date of the Notice, and will evaluate available options to resolve the deficiency and regain compliance. If our compliance plan is accepted, we may be granted up to 180 calendar days from April 7, 2022 to evidence compliance. There can be no assurance that we will be able to regain compliance with Nasdaq Listing Rule 5450(b)(1)(A), maintain compliance with any other listing requirements, or be able to transfer the listing of our common stock to the Nasdaq Capital Market.

In such circumstance, if we fail to regain compliance, our common stock will be subject to delisting. Delisting from Nasdaq could adversely affect our ability to raise additional financing through the public or private sale of equity securities, would significantly affect the ability of investors to trade our securities and would negatively affect the value and liquidity of our common stock. Delisting could also have other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest and fewer business development opportunities.

Unless our common stock continues to be listed on a national securities exchange it will become subject to the so-called "penny stock" rules that impose restrictive sales practice requirements.

If we are unable to maintain the listing of our common stock on Nasdaq or another national securities exchange, our common stock could become subject to the so-called "penny stock" rules if the shares have a market value of less than $5.00 per share. The SEC has adopted regulations that define a penny stock to include any stock that has a market price of less than $5.00 per share, subject to certain exceptions, including an exception for stock traded on a national securities exchange. The SEC regulations impose restrictive sales practice requirements on broker-dealers who sell penny stocks to persons other than established customers and accredited investors. An accredited investor generally is a person whose individual annual income exceeded $200,000, or whose joint annual income with a spouse exceeded $300,000 during the past two years and who expects their annual income to exceed the applicable level during the current year, or a person with net worth in excess of $1.0 million, not including the value of the investor's principal residence and excluding mortgage debt secured by the investor's principal residence up to the estimated fair market value of the home, except that any mortgage debt incurred by the investor within 60 days prior to the date of the transaction shall not be excluded from the determination of the investor's net worth unless the mortgage debt was incurred to acquire the residence. For transactions covered by this rule, the broker-dealer must make a special suitability determination for the purchaser and must have received the purchaser's written consent to the transaction prior to sale. This means that if we are unable maintain the listing of our common stock on a national securities exchange, the ability of stockholders to sell their common stock in the secondary market could be adversely affected. If a transaction involving a penny stock is not exempt from the SEC's rule, a broker-dealer must deliver a disclosure schedule relating to the penny stock market to each investor prior to a transaction. The broker-dealer also must disclose the commissions payable to both the broker-dealer and its registered representative, current quotations for the penny stock, and, if the broker-dealer is the sole market-maker, the broker-dealer must disclose this fact and the broker-dealer's presumed control over the market. Finally, monthly statements must be sent disclosing recent price information for the penny stock held in the customer's account and information on the limited market in penny stocks.

The holders of our Series A preferred stock have liquidation and other rights that are senior to the rights of the holders of shares of our common stock.

In the event of a merger, acquisition, liquidation, dissolution, or winding up of Calithera whether voluntary or involuntary, the holders of our Series A preferred stock will be entitled to have set apart for them, or to be paid, out of our assets available for distribution to stockholders after provision for payment of all of our debts and liabilities in accordance with the Delaware General Corporation Law, before any distribution or payment is made with respect to any shares of junior securities, including shares of our common stock, an amount per share equal to the greater of (i) $35.00, being the issuance price per share of Series A preferred stock, and (ii) such amount as would have been payable on the number of shares of common stock into which the shares of Series A preferred stock could have been converted immediately prior to such event. If applicable, this preference would reduce the amount of our assets, if any, available to distribute to holders of our common stock.

We may be required to issue a significant number of additional shares of common stock for no additional consideration to the holders of our Series A preferred stock pursuant to certain price-based anti-dilution provisions.

We may be required to issue a significant number of shares of common stock for no additional consideration to the holders of our Series A preferred stock, subject to certain beneficial ownership limitations described in the certificate of designations defining the rights of the holders of the Series A preferred stock. The terms of the Series A preferred stock provide that such shares will automatically convert into common stock on the earlier of: (i) the 18-month anniversary of the date of issuance, or the Mandatory Pricing Date, into 17,156,863 shares of common stock, subject to adjustment into additional shares of common stock if the volume weighted-average price of our common stock for the thirty trading days prior to the Mandatory Pricing Date is lower than $2.04 per share, and (ii) a qualified financing that results in net proceeds to us of at least $40.0 million, excluding any conversion of the Series A preferred stock, subject to adjustment into additional shares of common stock if the weighted-average price per paid by investors in

such qualified financing is lower than $2.04 per share. The holders of Series A preferred stock also have the option, at any time prior to the Mandatory Pricing Date or such qualified financing to convert the Series A preferred stock into shares of common stock, subject to adjustment into additional shares of common stock if the volume weighted-average sales price of certain shares of common stock are sold from the issuance date of the Series A preferred stock through the date of the written election at an effective price less than $2.04 per share.

Stockholders will incur dilution of their percentage ownership interest in our common stock to the extent we issue additional shares of common stock to the holders of the Series A preferred stock. Any issuance or potential issuance of additional shares of common stock could adversely affect our stock price, make it more difficult for us to raise capital on favorable terms, or at all, and harm our business, results of operations and financial condition.

We cannot take certain actions without the consent of the holders of Series A preferred stock.

Certain matters require the approval of the Series A preferred stock, voting as a separate class, including to:

- amend our organizational documents in a way that has an adverse effect on the Series A preferred stock;
- create or authorize the creation of any new security, or reclassify or amend any existing security, that are senior to, or equal in priority with, the Series A preferred stock, including any shares of Series A preferred stock, with respect to the distribution of assets on the liquidation, dissolution or winding up of Calithera, the payment of dividends and rights of redemption; or
- purchase or redeem, or pay or declare, any dividend or make any distribution on, any shares of our capital stock, subject to certain exceptions.

The interests of Millennium, the sole holder of our Series A preferred stock and those of the holders of common stock may be inconsistent, which may result in our inability to obtain the consent of the holders of Series A preferred stock to matters that may be in the best interests of the common stockholders.

We may be required to make significant cash payments to the holders of Series A preferred stock if we do not receive requisite stockholder approval to allow the conversion of the Series A preferred stock to common stock, which may limit our working capital liquidity.

As part of our acquisition of the Takeda Programs, if we are unable to obtain stockholder approval in accordance with the rules of The Nasdaq Stock Market LLC for the conversion of all of the shares of Series A preferred stock to common stock, and as a result Millennium is unable to convert any portion of the Series A preferred stock to common stock, we will be obligated under our purchase agreement with Millennium to negotiate in good faith as to the timing and form of consideration to compensate Millennium for such inability to convert. We are unable to estimate the actual amount or form of consideration we will be required to make at this time but we may become obligated to make significant cash payments to Millennium after three years following the purchase agreement date, which could limit our working capital liquidity. In addition, we may not have sufficient funds available to meet our obligations to Millennium, which may result in Millennium pursuing remedies under the purchase agreement that could adversely affect our operations.

We have granted Millennium registration rights with respect to the shares of common stock into which our Series A preferred stock is convertible. If these additional shares are sold, or it is perceived that they will be sold, the market price of our common stock could decline.

Millennium has the right, subject to some conditions, to require us to file a registration statement covering the resale of the shares of common stock issuable upon conversion of the Series A preferred stock. If we were to register the resale of these shares, they could be freely sold in the public market without limitation. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

The trading price of our common stock is likely to be volatile, and purchasers of our common stock could incur substantial losses.

Our stock price has fluctuated in the past and is likely to be volatile in the future. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may experience losses on their investment in our common stock. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- regulatory actions with respect to our product candidates or our competitors' product and product candidates;

- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- results of clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- actual and anticipated fluctuations in our quarterly operating results;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to in-license or acquire additional products or product candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- uncertainties regarding the magnitude and duration of impacts we are experiencing due to COVID-19;
- variations in our financial results or those of companies that are perceived to be similar to us;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- changes in the structure of healthcare payment systems;
- 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 addition, in the past, stockholders have initiated class action lawsuits against companies following periods of volatility in the market prices of these companies’ stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management’s attention and resources.

Concentration of ownership of our capital stock may prevent new investors from influencing significant corporate decisions.

Our executive officers, directors and current beneficial owners of 5% or more of our common stock, in the aggregate, beneficially own a significant percentage of our outstanding common stock. These persons, acting together, will be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors and any merger or other significant corporate transactions. The interests of this group of stockholders may not coincide with the interests of other stockholders.

Takeda, through its affiliate Millennium, beneficially owns a significant percentage of our total outstanding capital stock, which is initially convertible into 17,156,863 shares of our common stock, subject to price-based anti-dilution adjustments that if triggered would result in the issuance of additional shares of common stock. In no event will Takeda be entitled to cast votes in excess of, as of any date, 19.99% of our outstanding common stock. Takeda may be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors and any merger or other significant corporate transactions. The interests of Takeda may not coincide with the interests of other stockholders.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business, our market and our competitors. We do not have any control over these analysts. If one or more of the analysts who cover us downgrade our shares or change their opinion of our shares, our share price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

We have and will incur costs and demands upon management as a result of complying with the laws and regulations affecting public companies in the United States, which may harm our operating results.

As a public company listed in the United States, we have and will continue to incur significant additional legal, accounting and other expenses. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the Securities and Exchange Commission, or SEC, and the Nasdaq Global Select Market, may increase legal and financial compliance costs and make some activities more time-consuming. These laws, regulations and standards are subject to varying interpretations, and as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If, notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us, and our business may be harmed.

Further, failure to comply with these laws, regulations and standards might also make it more difficult for us to obtain certain types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our Board of Directors, on committees of our Board of Directors or as members of senior management.

We do not anticipate paying any cash dividends on our common stock so any returns will be limited to changes in the value of our common stock.

We have never declared or paid cash dividends on our common stock. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, the terms of any existing or future credit facility may restrict our ability to pay dividends. Any return to stockholders will therefore be limited to the increase, if any, of our stock price.

If we are unable to maintain proper and effective internal controls over financial reporting, the accuracy and timeliness of our financial reporting and the market price of our common stock may be adversely affected.

Effective internal controls are necessary for us to provide reliable financial reports and to protect from fraudulent, illegal or unauthorized transactions. If we cannot provide effective controls and reliable financial reports, our business and operating results could be harmed. We have in the past discovered, and may in the future discover, areas of our internal controls that need improvement. We are required, pursuant to Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on the effectiveness of our internal control over financial reporting. In the future, our independent registered public accounting firm may also need to attest to the effectiveness of our internal control over financial reporting.

If material weaknesses or control deficiencies occur in the future, we are unable to comply with the requirements of Section 404 in a timely manner, we are unable to assert that our internal control over financial reporting is effective, or if our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal control over financial reporting, we may be unable to report our financial results accurately on a timely basis, which could cause our reported financial results to be materially misstated and result in the loss of investor confidence and cause the market price of our common stock to decline.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management or hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by our stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, such as:

- establishing a classified Board of Directors so that not all members of our Board of Directors are elected at one time;
- permitting the Board of Directors to establish the number of directors and fill any vacancies and newly created directorships;
- providing that directors may only be removed for cause;
- prohibits cumulative voting for directors;
- requiring super-majority voting to amend some provisions in our certificate of incorporation and bylaws;

- authorizing the issuance of “blank check” preferred stock that our Board of Directors could use to implement a stockholder rights plan;
- eliminating the ability of stockholders to call special meetings of stockholders; and
- prohibiting stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibit a person who owns 15% or more 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. Any provision in our certificate of incorporation or our bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation designates the Court of Chancery of the State of Delaware and our amended and restated bylaws designate the federal district courts of the United States of America as the exclusive forums for substantially all disputes between us and our stockholders, which will restrict our stockholders' ability to choose the judicial forum for disputes with us or our directors, officers, or employees.*

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising under the Delaware General Corporation Law, our amended and restated certificate of incorporation or our bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine.

The provisions would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims.

To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid and several state trial courts have enforced such provisions and required that suits asserting Securities Act
claims be filed in federal court, there is no guarantee that courts of appeal will affirm the enforceability of such provisions and a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions. If a court were to find either exclusive forum provision in our amended and restated certificate of incorporation and/or our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with litigating Securities Act claims in state court, or both state and federal court, which could seriously harm our business, financial condition, results of operations, and prospects.

These exclusive choice of forum provisions may limit a stockholder’s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees. If a court were to find such exclusive-forum provisions to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

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

Recent Sales of Unregistered Equity Securities

On October 18, 2021, we issued 1,000,000 shares of Series A Preferred Stock to Millennium Pharmaceuticals, Inc., or Millennium, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, or Takeda. We issued the Series A Preferred Stock in reliance on the exemption from the registration requirements of the Securities Act of 1933, as amended, or the Securities Act, by virtue of Section 4(a)(2) thereof. In connection with Millennium’s execution of the Purchase Agreement, Millennium represented to us that they are an “accredited investor” as defined in Regulation D of the Securities Act and that the Series A Preferred Stock to be purchased by them will be acquired solely for their own account and for investment purposes and not with a view to the future sale or

distribution. The issuance and sale of the Series A Preferred Stock have not been registered under the Securities Act or the securities laws of any other jurisdiction, and such securities may not be offered or sold in the United States absent registration or an applicable exemption from registration requirements.

Use of Proceeds

None.

Issuer Purchases of Equity Securities

None.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

None.

Item 6. Exhibits

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed Herewith
		Form	SEC File No.	Exhibit	Filing Date	
3.1	Amended and Restated Certificate of Incorporation of Calithera Biosciences, Inc.	8-K	001-36644	3.1	10/7/2014	
3.2	Amended and Restated Bylaws of Calithera Biosciences, Inc.	10-Q	001-36644	3.2	8/10/2020	
3.3	Calithera Biosciences, Inc. Certificate of Designations of Preferences, Rights and Limitations of Series A Preferred Stock.	8-K	001-36644	3.1	10/19/2021	
4.1	Reference is made to Exhibits 3.1 through 3.3.					
4.2	Form of common stock certificate.	S-1	333-198355	4.1	9/25/2014	
4.3	Form of Short-Term Warrant.	8-K	001-36644	4.1	03/31/2022	
4.4	Form of Long-Term Warrant.	8-K	001-36644	4.2	03/31/2022	
4.5	Form of Warrant Agency Agreement by and between Calithera Biosciences, Inc. and American Stock Transfer & Trust Company.	8-K	001-36644	4.3	03/31/2022	
10.1^	Preferred Stock Purchase Agreement, by and between Calithera Biosciences, Inc. and Millennium Pharmaceuticals, Inc., dated as of October 18, 2021.	8-K	001-36644	10.1	10/19/2021	
10.2†#	Asset Purchase Agreement, between Calithera Biosciences, Inc. and Millennium Pharmaceuticals, Inc., dated as of October 18, 2021.	10-Q	001-36644	10.3	11/9/2021	
10.3	Sales Agreement, by and between Calithera Biosciences, Inc. and Jefferies LLC, dated August 10, 2020.	S-3	333-243731	1.2	8/10/2020	
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a).					X
31.2	Certification of Principal Financial and Accounting Officer pursuant to Rule 13a-14(a).					X
32.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2	Certification of Principal Financial and Accounting Officer pursuant to Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101 INS**	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.					
101 SCH**	Inline XBRL Taxonomy Extension Schema Document.					
101 CAL**	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					
101 DEF**	Inline XBRL Taxonomy Extension Definition Linkbase Document.					

101 LAB**	Inline XBRL Taxonomy Extension Label Linkbase Document.
101 PRE**	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104	The cover page from the Company's Quarterly Report on Form 10-Q for the three ended March 31, 2022, has been formatted in Inline XBRL.

* The certifications attached as Exhibit 32.1 and 32.2 that accompany this Quarterly Report on Form 10-Q are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of Calithera Biosciences, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Quarterly Report on Form 10-Q, irrespective of any general incorporation language contained in such filing.

** Attached as Exhibit 101 to this Quarterly Report on Form 10-Q for the quarter ended March 31, 2022 formatted in Inline XBRL (Extensible Business Reporting Language): (i) Condensed Consolidated Balance Sheets, (ii) Condensed Consolidated Statements of Operations, (iii) Condensed Consolidated Statements of Comprehensive Loss, (iv) Condensed Consolidated Statements of Stockholders' (Deficit) Equity, (v) Condensed Consolidated Statements of Cash Flows, and (vi) Notes to Condensed Consolidated Financial Statements, tagged as blocks of text and including detailed tags.

† Pursuant to a request for confidential treatment, portions of this Exhibit have been redacted from the publicly filed document and have been furnished separately to the Securities and Exchange Commission.

Certain portions of this agreement have been omitted pursuant to Item 601(b)(2) of Regulation S-K.

^ Certain portions of this agreement have been omitted pursuant to Item 601(a)(5) of Regulation S-K.

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.

Calithera Biosciences, Inc.

Date: May 10, 2022

By: /s/ Susan M. Molineaux

Susan M. Molineaux, Ph.D.

President and Chief Executive Officer

(Principal Executive Officer)

Date: May 10, 2022

By: /s/ Stephanie Wong

Stephanie Wong

Chief Financial Officer and Secretary

(Principal Financial and Accounting Officer)

EXHIBIT 31.1

CERTIFICATIONS

I, Susan M. Molineaux, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: May 10, 2022

/s/ Susan M. Molineaux

Susan M. Molineaux, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATIONS

I, Stephanie Wong, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: May 10, 2022

/s/ Stephanie Wong
Stephanie Wong
Chief Financial Officer and Secretary
(Principal Financial and Accounting Officer)

EXHIBIT 32.1

CALITHERA BIOSCIENCES, INC.
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 of Calithera Biosciences, Inc. (the "Company") on Form 10-Q for the quarter ended March 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Susan M. Molineaux, President and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

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

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

Date: May 10, 2022

/s/ Susan M. Molineaux
Susan M. Molineaux, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Calithera Biosciences, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.

Exhibit 32.2

CALITHERA BIOSCIENCES, INC.
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 of Calithera Biosciences, Inc. (the "Company") on Form 10-Q for the quarter ended March 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Stephanie Wong, Chief Financial Officer and Secretary of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

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

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

Date: May 10, 2022

/s/ Stephanie Wong
Stephanie Wong
Chief Financial Officer and Secretary
(Principal Financial and Accounting Officer)

This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Calithera Biosciences, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.