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 September 30, 2021

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 November 4, 2021, the registrant had 74,926,064 shares of common stock, $0.0001 par value per share, outstanding.

Calithera Biosciences, Inc.

Quarterly Report on Form 10-Q

For the Quarter Ended September 30, 2021

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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)

	September 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 84,493	$ 107,146
Short-term investments	—	8,005
Receivables from collaborations	12	1,541
Prepaid expenses and other current assets	1,829	2,011
Total current assets	86,334	118,703
Restricted cash	270	440
Property and equipment, net	622	690
Operating lease right-of-use asset	2,745	5,754
Total assets	$ 89,971	$ 125,587
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,971	$ 1,994
Accrued and other liabilities	10,559	16,407
Total current liabilities	13,530	18,401
Noncurrent operating lease liability	2,022	4,815
Total liabilities	15,552	23,216
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.0001 par value, 200,000 shares authorized as of September 30, 2021, and December 31, 2020; 74,114 and 70,686 shares issued and outstanding as of September 30, 2021, and December 31, 2020, respectively	7	7
Additional paid-in capital	496,528	478,599
Accumulated deficit	(422,116)	(376,238)
Accumulated other comprehensive income	—	3
Total stockholders' equity	74,419	102,371
Total liabilities and stockholders' equity	$ 89,971	$ 125,587

See accompanying notes.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Revenue:				
License revenue	$ 6,750	$ —	$ 9,750	$ —
Total revenue	6,750	—	9,750	—
Operating expenses:				
Research and development	11,556	18,157	39,715	53,938
General and administrative	6,344	4,744	16,259	14,786
Total operating expenses	17,900	22,901	55,974	68,724
Loss from operations	(11,150)	(22,901)	(46,224)	(68,724)
Interest and other income (expense), net	(22)	167	346	1,153
Net loss	$ (11,172)	$ (22,734)	$ (45,878)	$ (67,571)
Net loss per share, basic and diluted	$ (0.15)	$ (0.32)	$ (0.62)	$ (0.99)
Weighted average common shares used to compute net loss per share, basic and diluted	74,114	70,559	73,480	68,219

See accompanying notes.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Net loss	$ (11,172)	$ (22,734)	$ (45,878)	$ (67,571)
Other comprehensive income (loss):				
Net unrealized gain (loss) on available-for-sale securities	—	(71)	(3)	4
Total comprehensive loss	$ (11,172)	$ (22,805)	$ (45,881)	$ (67,567)

See accompanying notes.

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

	Three Months Ended September 30, 2021					
	Common Stock					
	Shares	Amount	Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Equity
Balance at June 30, 2021	74,113	$ 7	$ 493,950	$ (410,944)	$ —	$ 83,013
Exercise of stock options	1	—	1	—	—	1
Stock-based compensation expense	—	—	2,577	—	—	2,577
Net loss	—	—	—	(11,172)	—	(11,172)
Balance at September 30, 2021	74,114	$ 7	$ 496,528	$ (422,116)	$ —	$ 74,419

	Three Months Ended September 30, 2020					
	Common Stock					
	Shares	Amount	Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Equity
Balance at June 30, 2020	70,559	$ 7	$ 474,098	$ (330,938)	$ 117	$ 143,284
Stock-based compensation expense	—	—	2,117	—	—	2,117
Net loss	—	—	—	(22,734)	—	(22,734)
Unrealized loss on available-for-sale securities	—	—	—	—	(71)	(71)
Balance at September 30, 2020	70,559	$ 7	$ 476,215	$ (353,672)	$ 46	$ 122,596

See accompanying notes

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

	Nine Months Ended September 30, 2021					
	Common Stock					
	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	3,361	—	9,888	—	—	9,888
Exercise of stock options	7	—	7	—	—	7
Issuance of common stock per employee stock plan purchases	60	—	118	—	—	118
Stock-based compensation expense	—	—	7,916	—	—	7,916
Net loss	—	—	—	(45,878)	—	(45,878)
Unrealized loss on available-for-sale securities	—	—	—	—	(3)	(3)
Balance at September 30, 2021	74,114	$ 7	$ 496,528	$ (422,116)	$ —	$ 74,419

	Nine Months Ended September 30, 2020					
	Common Stock					
	Shares	Amount	Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Equity
Balance at December 31, 2019	63,514	$ 6	$ 428,479	$ (286,101)	$ 42	$ 142,426
Issuance of common stock in connection with public offering, net of underwriting commissions and issuance costs	5,750	1	33,463	—	—	33,464
Issuance of common stock in connection with at-the-market offering, net of underwriting commissions and issuance costs	1,160	—	7,397	—	—	7,397
Exercise of stock options	33	—	314	—	—	314
Issuance of common stock per employee stock plan purchases	102	—	386	—	—	386
Stock-based compensation expense	—	—	6,176	—	—	6,176
Net loss	—	—	—	(67,571)	—	(67,571)
Unrealized gain on available-for-sale securities	—	—	—	—	4	4
Balance at September 30, 2020	70,559	$ 7	$ 476,215	$ (353,672)	$ 46	$ 122,596

See accompanying notes.

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

	Nine Months Ended September 30,	
	2021	**2020**
Cash Flows Used in Operating Activities		
Net loss	$ (45,878)	$ (67,571)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	215	282
Accretion (amortization) of premiums and discounts on investments	2	(160)
Stock-based compensation	7,916	6,176
Gain on remeasurement of the lease liability	(362)	—
Non-cash lease expense	867	1,116
Changes in operating assets and liabilities:		
Receivables from collaborations	1,529	16
Prepaid expenses and other current assets	182	184
Other assets	—	(64)
Accounts payable	938	524
Accrued liabilities	(5,282)	(772)
Lease liability	(855)	(1,042)
Net cash used in operating activities	(40,728)	(61,311)
Cash Flows Provided by (Used in) Investing Activities		
Purchases of investments	—	(57,061)
Proceeds from sale and maturity of investments	8,000	136,981
Purchases of property and equipment	(108)	(25)
Net cash provided by investing activities	7,892	79,895
Cash Flows Provided by Financing Activities		
Proceeds from issuance of common stock upon public offering, net	—	33,464
Proceeds from issuance of common stock through an at-the-market offering, net	9,888	7,397
Proceeds from stock option exercises and employee stock purchase plan purchases	125	700
Net cash provided by financing activities	10,013	41,561
Net (decrease) increase in cash, cash equivalents, and restricted cash	(22,823)	60,145
Cash, cash equivalents, and restricted cash at beginning of period	107,586	60,877
Cash, cash equivalents, and restricted cash at end of period	$ 84,763	$ 121,022

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.

Liquidity

In the course of its development activities, the Company has sustained operating losses and expects such losses to continue over the next several years. The Company's ultimate success depends on the outcome of its research and development activities. The Company has incurred net losses from operations since inception and has an accumulated deficit of $422.1 million as of September 30, 2021. The Company intends to raise additional capital through the issuance of additional equity, and potentially through strategic alliances with partner companies. However, if such financing is not available at adequate levels, the Company will need to reevaluate its operating plans. Management believes that the currently available resources will provide sufficient funds to enable the Company to meet its operating plan for at least the twelve-month period following the filing of the Company's unaudited consolidated financial statements for the three and nine months ended September 30, 2021, included in the Quarterly Report on Form 10-Q. However, if the Company's anticipated operating results are not achieved in future periods, management believes that planned expenditures may need to be reduced in order to extend the time period over which the then-available resources would be able to fund the Company's operations.

2. Summary of Significant Accounting Policies

Unaudited Interim Financial Information

The interim condensed consolidated balance sheet as of September 30, 2021, the statements of operations, comprehensive loss, and stockholders' equity, for the three and nine months ended September 30, 2021 and 2020, and the statement of cash flows for the nine months ended September 30, 2021 and 2020 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 and nine-month periods are also unaudited. The results of operations for the three and nine months ended September 30, 2021 are not necessarily indicative of the results to be expected for the year ending December 31, 2021 or for any other future annual or interim period. The balance sheet as of December 31, 2020 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 September 30, 2021 and December 31, 2020.

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 ASU No. 2016-02, *Leases (Topic 842)*, or ASU 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 Recently Adopted

In December 2019, the FASB issued Accounting Standards Update ("ASU") No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*, which removes certain exceptions and amends certain requirements in the existing

income tax guidance to ease accounting requirements. This guidance is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020 and must be applied on a retrospective basis. The Company adopted this guidance effective January 1, 2021 and there was no impact on its consolidated financial statements and disclosures.

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 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 from collaborations, 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):

	September 30, 2021			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 80,830	$ —	$ —	$ 80,830
Total financial assets	$ 80,830	$ —	$ —	$ 80,830

	December 31, 2020			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 106,782	$ —	$ —	$ 106,782
Corporate notes and commercial paper	—	6,502	—	6,502
U.S. government agency securities	—	1,503	—	1,503
Total financial assets	$ 106,782	$ 8,005	$ —	$ 114,787

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):

	September 30, 2021				December 31, 2020			
	Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value	Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value
Money market funds	$ 80,830	$ —	$ —	$ 80,830	$ 106,782	$ —	$ —	$ 106,782
Corporate notes and commercial paper	—	—	—	—	6,501	1	—	6,502
U.S. government agency securities	—	—	—	—	1,501	2	—	1,503
	$ 80,830	$ —	$ —	$ 80,830	$ 114,784	$ 3	$ —	$ 114,787
Classified as:								
Cash equivalents				$ 80,560				$ 106,342
Short-term investments				—				8,005
Restricted cash				270				440
Total cash equivalents, restricted cash and investments				$ 80,830				$ 114,787

At September 30, 2021, the remaining contractual maturities of available-for-sale securities were less than one year. There have been no significant realized gains or losses on available-for-sale securities for the periods presented. As of September 30, 2021 and December 31, 2020, there were no unrealized losses on cash equivalents and investments. As of September 30, 2021, the Company had a total of $84.8 million in cash, cash equivalents and restricted cash, which includes approximately $4.0 million in cash and $80.8 million in cash equivalents and restricted cash.

5. Accrued and Other Liabilities

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

	September 30, 2021	December 31, 2020
Accrued clinical and manufacturing expenses	$ 4,485	$ 7,910
Accrued payroll and related expenses	3,874	5,142
Current portion of lease liability	1,338	1,903
Other	862	1,452
Total accrued and other liabilities	$ 10,559	$ 16,407

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 2.3 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. In addition, the Company had a non-cancelable sublease agreement for a portion of its facilities through February 2020. The sublease agreement provided that the subtenant was obligated to pay its share of the variable costs under the Lease. Through March 7, 2021 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 nine months ended September 30, 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 and nine months ended September 30, 2021 and 2020, were as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
Operating Lease Costs:	**2021**	**2020**	**2021**	**2020**
Straight-line rent expense related to facility operating lease	$ 326	$ 544	$ 1,136	$ 1,633
Variable rent expense related to facility operating lease	260	381	753	1,128
Sublease income	—	—	—	(187)
Variable sublease income	—	—	—	(93)
Net operating lease costs	$ 586	$ 925	$ 1,889	$ 2,481

Cash paid for amounts included in the measurement of the lease liabilities for both the three months ended September 30, 2021 and 2020, was $0.4 million and was included in net cash used in operating activities in the Company's unaudited condensed consolidated statements of cash flows. Cash paid for amounts included in the measurement of the lease liabilities for the nine months ended September 30, 2021 and 2020, was $1.1 million and $1.6 million, respectively, and 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:	**September 30, 2021**	**December 31, 2020**
Current portion included in accrued and other liabilities	$ 1,338	$ 1,903
Noncurrent operating lease liability	2,022	4,815
Total operating lease liability	$ 3,360	$ 6,718

The maturities of the Company's lease liability as of September 30, 2021, was as follows (in thousands):

Year ending December 31:	
2021 (excluding the nine months ended September 30, 2021)	$ 379
2022	1,546
2023	1,593
2024	136
Total lease payments	3,654
Less: interest	(294)
Present value of lease liability	$ 3,360

7. Stockholders' 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 $75.0 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 nine months ended September 30, 2021, the Company sold 3,361,202 shares under the ATM program at an average price per share of $3.02, for net proceeds of $9.9 million. As of September 30, 2021, a total of 3,361,202 shares had been sold under the ATM program.

8. 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, 2020	8,637	$ 6.91		
Options granted	2,007	$ 2.90		
Options exercised	(7)	$ 0.96		
Options cancelled	(1,982)	$ 6.22		
Outstanding — September 30, 2021	8,655	$ 6.14	6.74	$ 25
Exercisable — September 30, 2021	5,342	$ 7.16	5.52	$ 24

Stock Awards

During the nine months ended September 30, 2021, the Company issued 558,406 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 vest 20% on January 3, 2022 and 80% upon the achievement of two goals that are expected to be 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 estimates that all vesting conditions are probable of being achieved and has 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 will monitor the probability of achievement of the goals each reporting period and adjust its estimates accordingly. During the three and nine months ended September 30, 2021, the Company recorded $1.0 million and $2.9 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, 2020	—	$ —		
PSUs and RSUs — Awarded	2,166	$ 2.96		
PSUs and RSUs — Cancelled	(339)	$ 2.98		
Outstanding — September 30, 2021	1,827	$ 2.96	1.02	$ 3,982

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 September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Research and development	$ 1,459	$ 1,070	$ 4,327	$ 3,232
General and administrative	1,118	1,047	3,589	2,944
Total stock-based compensation	$ 2,577	$ 2,117	$ 7,916	$ 6,176

9. 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):

	September 30,	
	2021	2020
Options to purchase common stock	8,655	8,659
Employee stock plan purchases	59	73
Restricted stock units subject to future vesting	1,827	—
Total	10,541	8,732

10. 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 $45.0 million in February 2017. In March 2017, the Company achieved a development milestone of $12.0 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 $18.0 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 September 30, 2021 were $720.0 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.

In accordance with ASC 606, the Company determined the transaction price to be $57.0 million, representing the $45.0 million upfront payment and the $12.0 million developmental milestone payment from Incyte that was earned in March 2017. The $57.0 million transaction price was recognized over the estimated performance period, based on the measure of progress toward completion for the combined performance obligation, which was satisfied as of June 2018. The measure of progress towards completion was based on the effort of certain employees within the Company who dedicated time to complete the manufacturing services and technology transfer to Incyte.

Net costs associated with co-development activities performed under the agreement are included in research and development expenses in the accompanying unaudited condensed consolidated statements of operations, with any reimbursement of costs by Incyte reflected as a reduction of such expenses. For the three months ended September 30, 2021 and 2020, net costs payable to Incyte were approximately $2,000 and $0.3 million, respectively. For the nine months ended September 30, 2021 and 2020, net costs payable to Incyte were $16,000 and $0.3 million, respectively. As of September 30, 2021, net amounts payable to Incyte were $0.4 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 $3.0 million in May 2021 and may receive potential development, regulatory and sales milestones of up to $252.0 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 $3.0 million during the three months ended June 30, 2021. No revenue was recognized during the three months ended September 30, 2021 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 and nine months ended September 30, 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.

11. 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 and nine months ended September 30, 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.

12. Reduction in Workforce

On January 4, 2021, the Company announced a plan to reduce its workforce by approximately 35% to extend its cash runway and ensure long-term sustainability. During the three-month period ended September 30, 2021, the Company recognized ($25,000) and $0 of severance-related charges to research and development and general and administrative expenses, respectively, which is included in operating expenses in the unaudited condensed consolidated statements of operations. During the nine-month period ended September 30, 2021, the Company recognized $1.0 million and $0.2 million of severance-related charges to research and development and general and administrative expenses, respectively, which is included in operating expenses in the unaudited condensed consolidated statements of operations. As of September 30, 2021, the Company had recognized substantially all expenses related to the workforce reduction.

A summary of activity in the accrued liability associated with the Company's reduction in workforce for the nine months ended September 30, 2021 was as follows (in thousands):

	Severance Costs Related to Reduction in Workforce
Accrued balance as of January 1, 2021	$ —
Charges	1,156
Cash payments	(1,143)
Accrued balance as of September 30, 2021	$ 13

13. Subsequent Event

Takeda Asset Purchase Agreement

On October 18, 2021, the Company entered into an Asset Purchase Agreement, or the 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 $10.0 million in cash and issued to Millennium 1,000,000 shares of its Series A Convertible Preferred Stock as referenced below. 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 $470.0 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 to Millennium 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 from October 15, 2021. The conversion rate of the Series A Convertible 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 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. If the Company is 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 by the three year anniversary date of the issuance of the Series A Preferred Stock (as a result of certain beneficial ownership limitations), then the Company 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 the Company is 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.

The Company intends to seek stockholder approval at its 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 is also subject to certain preferences, rights and limitations.

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 (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 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, we are advancing a robust 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. While we are primarily focused on oncology, we are opportunistically developing therapeutics outside of oncology where we can leverage our existing expertise in immune cell metabolism to treat diseases with unmet needs, as is the case in cystic fibrosis.

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.

In October 2021, we entered into an Asset Purchase Agreement, or the 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 with the greatest potential in biomarker-defined cancer patient populations. The compounds, sapanisertib (CB-228, formerly TAK-228) and mivavotinib (CB-659, formerly TAK-659), 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 include leveraging our clinical and biomarker expertise in the KEAP1/NRF2 pathway by developing our mTORC1/2 inhibitor sapanisertib in squamous non-small cell lung cancer, and advancing the development of our SYK inhibitor mivavotinib in specific biomarker-defined populations of diffuse large B-cell lymphoma, or DLBCL. 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 over the next 12 to 18 months.

Sapanisertib is a dual TORC 1/2 inhibitor that targets a key survival mechanism in KEAP1/NRF2-mutated tumor cells. These mutations are found in a considerable sub-population of patients across multiple solid tumor types. In squamous non-small cell lung

cancer, NRF2 mutations occur in approximately 15% of patients, and KEAP mutations occur in approximately 12% of patients. Sapanisertib has demonstrated promising single-agent activity in patients with relapsed/refractory NRF2-mutated squamous non-small cell lung cancer and exhibits differential anti-tumor activity compared to rapalog inhibitors of TORC1 in NRF2-mutant squamous NSCLC xenograft models. Sapanisertib has a well-characterized clinical safety profile and was well tolerated in relapsed/refractory NSCLC patients. Of the greater than 235,000 people diagnosed with NSCLC in the US each year, approximately 25-30% of those are squamous NSCLC. Actionable mutations are only found in 1-5% of squamous NSCLC patients, leaving few options after PD-1 inhibitors and chemotherapy. The standard-of-care chemotherapy options in relapsed/refractory squamous NSCLC have a median PFS of 3-4.5 months. Because NRF2/KEAP1 mutations confer a poorer prognosis for NSCLC patients, sapanisertib has the potential to address a substantial underserved patient population. A Phase 2 study planned to begin in the first quarter of 2022 will strengthen the existing data on sapanisertib as a monotherapy in patients with squamous NSCLC harboring a NRF2 mutation and further evaluate its monotherapy in KEAP1 mutated and NRF2/KEAP1 wild-type squamous NSCLC. Data generated over the next 12 to 18 months from this study could position the company to initiate a registrational study in squamous NSCLC. Additional development plans may include exploring the potential of sapanisertib in KEAP1/NRF2 mutant tumor types beyond NSCLC.

Sapanisertib has been granted composition of matter patent protection that would extend through 2036 in the U.S. and through 2034 in the E.U., assuming a full 5-year patent term extension.

Mivavotinib is a SYK inhibitor that targets the constitutively activated BCR pathway in many non-Hodgkin's lymphoma (NHL) cases, including those harboring CD79 mutations, and also targets the inflammatory signaling pathway that is constitutively active in MyD88-mutated NHL. In completed Phase 1/2 clinical trials mivavotinib showed promising single-agent responses with deep and durable single agent activity in unselected 3L+ DLBCL and other NHLs. Mivavotinib demonstrated higher ORR/DOR than other SYK inhibitors in DLBCL clinical trials. The overall safety profile of mivavotinib appears favorable for further development as a single agent and in combination with standard of care therapies. In addition, recent preclinical studies have shown enhanced SYK activity and sensitivity to SYK inhibition in DLBCL and other NHLs harboring mutations in MyD88 and/or CD79, which comprise a distinct genetic subset of DLBCL known to have poor outcomes with standard-of-care therapy.

DLBCL represents the most common subtype of NHL, and represents approximately 30% of all NHL cases. Thirty-thousand people are diagnosed in the US each year with an approximately 60% 5-year survival rate. MyD88 mutations occur in approximately 30%, and CD79 mutations occur in 10-15%, of all DLBCL cases.

We plan to initiate a Phase 2 study of mivavotinib in the first quarter of 2022 for the treatment of patients with DLBCL with and without mutations in MyD88 and CD79. Data generated over the next 12 to 18 months from this study would position the company to initiate a study with registrational intent in biomarker-specific populations in DLBCL. Beyond DLBCL, both preclinical and clinical data support expansion across additional NHL subtypes and other hematologic malignancies as part of long-term plans. Additional development plans may include generating data in Waldenstrom macroglobulinemia and other NHL with MyD88/CD79 mutations, and exploring combinations with standard of care agents such as ibrutinib, venetoclax, and anti-CD20 in NHL.

Mivavotinib has been granted composition of matter patent protection through 2036 in the U.S. and through 2035 in the E.U., assuming a full 5-year patent term extension.

Pursuant to the APA, in October 2021, we paid Millennium an upfront payment of $10.0 million in cash and issued to Millennium 1,000,000 shares of its Series A Convertible Preferred Stock at a valuation of $2.04 per equivalent one share of Common Stock, for an aggregate deemed issue price of $35.0 million. We 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 $470.0 million in clinical development, regulatory and sales milestone payments across both programs.

Our product candidate, CB-280, which is solely owned by Calithera, is a novel oral inhibitor of arginase being developed for the treatment of cystic fibrosis, or CF. In October 2020, we were awarded up to $2.4 million from the Cystic Fibrosis Foundation to support development of CB-280. Arginase is secreted by infiltrating neutrophils in the lungs of CF patients and depletes the amino acid arginine. Arginine is critical for the generation of sufficient nitric oxide, or NO, to maintain anti-microbial effects and bronchodilation in the lungs of CF patients. According to third-party market research, there are over 70,000 people living with CF, over 30,000 of those are in the US. By 2026, worldwide sales for CF drugs are expected to surpass $11 billion. We completed a Phase 1 Single Ascending Dose trial to evaluate the safety, tolerability and pharmacokinetic profile of oral CB-280 in healthy volunteers. In July 2020, we initiated a Phase 1b clinical trial in adult patients with cystic fibrosis that are on a stable regimen of CF therapies and have chronic airway infection. The randomized, double blind, placebo-controlled, dose escalation trial is evaluating multiple ascending doses of CB-280, dosed orally twice daily for 14 days, compared to placebo in up to 32 adult CF patients to determine a safe dose range for CB-280.

In November 2021, we presented interim data from the Phase 1b trial at the North American Cystic Fibrosis Conference. Data were presented on the first 24 subjects (18 treated with CB-280, six with placebo) participating in the ongoing, Phase 1b dose-escalation trial in adults with CF. Key eligibility criteria for patients included chronic lung infection and current treatment with a stable CF medication regimen including cystic fibrosis transmembrane conductance regulator (CFTR) modulators. Each dose cohort consisted of eight subjects randomized 3:1 to CB-280 or placebo dosed twice daily for 14 days. At the completion of each dose cohort, unblinded data were reviewed by an Independent Data Safety Monitoring Committee (IDMC) convened by the Cystic Fibrosis Foundation (CFF).

Data were presented for 50mg BID, 100mg BID and 200mg BID dose levels. The study enrolled subjects with a broad spectrum of CFTR genotypes, including nonsense mutations. Notably, 91% of subjects were already on CFTR modulator therapy with Trikafta® (elexacaftor/tezacaftor/ivacaftor) or Kalydeco®(ivacaftor). CB-280 had a well-tolerated safety profile across all three dose levels, and all 18 subjects receiving CB-280 completed treatment without treatment interruptions or premature discontinuations. CB-280 demonstrated linear pharmacokinetics with plasma exposure increasing proportionally with dose. Complete and continuous target inhibition in plasma was achieved at the 100 mg dose and above. CB-280 also demonstrated robust pharmacodynamic effects, with rapid and significant dose-proportional increases in plasma arginine, the key driver of NO production. Increased airway NO production was reflected by a trend showing an increase in fractional exhaled nitric oxide (FeNO) in subjects treated with CB-280. Sweat chloride, a marker of CFTR function, showed a trend towards decreasing in CB-280 treated subjects, in line with previously reported preclinical data showing that arginase inhibition enhances CFTR function in human bronchial epithelial cells. Together, these biomarker trends further substantiate the proposed mechanism of action as a rational approach to treating CF. Changes in forced expiratory volume in one second (FEV1) were assessed as a safety endpoint. A pooled analysis of treatment vs. placebo showed a positive trend in FEV1 compared to placebo. Dose escalation is ongoing, with Cohort 4 (300mg BID) and on track to complete enrollment by the end of the year, with the option for an additional dose cohort to enroll in 2022 if warranted.

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 as a monotherapy and in combination with other anti-cancer agents. In January 2017, we entered into a collaboration and license agreement, or the Incyte Collaboration Agreement, with Incyte. Under the terms of the Incyte Collaboration Agreement, we granted Incyte an exclusive, worldwide license to co-develop and co-commercialize our small molecule arginase inhibitors for hematology and oncology indications. In April 2020, we 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 $18.0 million we believed were due under the Incyte Collaboration Agreement. In September 2021, we 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, we received and recognized the $6.75 million as milestone revenues. Effective September 30, 2020, we opted out of our co-development obligations as permitted under the terms of the Incyte Collaboration Agreement. As a result of our decision to opt out, Incyte will pay all costs to develop INCB001158 or any other licensed products. Incyte will pay us tiered royalties ranging from the low double digits to mid-teens on net sales of licensed products and total remaining potential development, regulatory and commercialization milestones of $720.0 million.

Another area of research interest has been immune-modulatory enzymes. We have developed CB-708, a highly potent, selective, orally-bioavailable small molecule inhibitor of CD73. Preclinical data were presented at the 2019 American Association for Cancer Research annual meeting and the 2019 Society for Immunotherapy of Cancer meeting demonstrating that CB-708 has immune-mediated, single agent activity in syngeneic mouse tumor models. In pre-clinical studies CB-708 was well tolerated and shows enhanced anti-tumor activity when combined with either an anti-PD-L1 immunotherapy or with chemotherapeutic agents, such as oxaliplatin or doxorubicin. 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. Under the terms of the license agreement, we received an upfront payment of $3.0 million in May 2021 and may receive potential development, regulatory and sales milestone of up to $252.0 million. Additionally, we are eligible to receive tiered royalties on sales of licensed product up to low double-digits.

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 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.

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

In addition, Calithera continues to leverage its discovery engine to build a robust preclinical pipeline of undisclosed synthetic lethality targets with a focus on paralog genes. These will be announced as we advance preclinical development.

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, 2020, as filed with the SEC.

Financial Overview

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; and
- license fees and milestone payments related to our licensing agreements.

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 and nine months ended September 30, 2021 and 2020:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands)			
Development candidate:				
Telaglenastat (CB-839)	$ 6,752	$ 13,325	$ 27,509	$ 39,475
INCB001158	—	1,253	—	4,073
CB-280	1,989	1,965	5,536	5,008
Total development	8,741	16,543	33,045	48,556
Preclinical and research:				
Preclinical and research	2,815	1,614	6,670	5,382
Total	$ 11,556	$ 18,157	$ 39,715	$ 53,938

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 September 30, 2021 and 2020

	Three Months Ended September 30,		Change	
	2021	2020	$	%
	(in thousands, except percentages)			
Revenue:				
License revenue	$ 6,750	$ —	$ 6,750	N/A
Total revenue	6,750	—	6,750	N/A
Operating expenses:				
Research and development	11,556	18,157	(6,601)	-36%
General and administrative	6,344	4,744	1,600	34%
Total operating expenses	17,900	22,901	(5,001)	-22%
Loss from operations	(11,150)	(22,901)	11,751	-51%
Interest and other income (expense), net	(22)	167	(189)	-113%
Net loss	$ (11,172)	$ (22,734)	$ 11,562	-51%

License Revenue. License revenue increased from $0 for the three months ended September 30, 2020 to $6.8 million for the three months ended September 30, 2021, and represents the milestone payment received in September 2021 under our Incyte Collaboration Agreement.

Research and Development. Research and development expenses decreased $6.6 million, or 36%, from $18.2 million for the three months ended September 30, 2020 to $11.6 million for the three months ended September 30, 2021. The decrease of $6.6 million was due to a $6.6 million decrease in the telaglenastat program and a $1.2 million decrease in the INCB001158 program, partially offset by a $1.2 million increase in our early stage research.

General and Administrative. General and administrative expenses increased $1.6 million, or 34%, from $4.7 million for the three months ended September 30, 2020, to $6.3 million for the three months ended September 30, 2021. The increase was primarily due to an increase in legal expenses related to our Settlement Agreement and Release with Incyte and our Asset Purchase Agreement with Takeda.

Interest and Other Income (expense), net. Interest and other income (expense), net decreased $0.2 million, or 113%, from $0.2 million for the three months ended September 30, 2020 to ($22,000) for the three months ended September 30, 2021. The decrease of $0.2 million was primarily due to lower interest income generated from lower returns and lower balances on our investments.

Comparison of the Nine Months Ended September 30, 2021 and 2020

	Nine Months Ended September 30,		Change	
	2021	2020	$	%
	(in thousands, except percentages)			
Revenue:				
License revenue	$ 9,750	$ —	$ 9,750	N/A
Total revenue	9,750	—	9,750	N/A
Operating expenses:				
Research and development	39,715	53,938	(14,223)	-26%
General and administrative	16,259	14,786	1,473	10%
Total operating expenses	55,974	68,724	(12,750)	-19%
Loss from operations	(46,224)	(68,724)	22,500	-33%
Interest and other income (expense), net	346	1,153	(807)	-70%
Net loss	$ (45,878)	$ (67,571)	$ 21,693	-32%

License Revenue. License revenue increased from $0 for the nine months ended September 30, 2020 to $9.8 million for the nine months ended September 30, 2021 and represents the $6.75 million milestone payment received in September 2021 under our Incyte Collaboration Agreement and the recognition of the $3.0 million upfront payment received in May 2021 from the Antengene License Agreement.

Research and Development. Research and development expenses decreased $14.2 million, or 26%, from $53.9 million for the nine months ended September 30, 2020 to $39.7 million for the nine months ended September 30, 2021. The decrease of $14.2 million was due to an $11.9 million decrease in the telaglenastat program and a $4.1 million decrease in the INCB001158 program, partially offset by a $1.3 million increase in our early stage research and a $0.5 million increase in the CB-280 program.

General and Administrative. General and administrative expenses increased $1.5 million, or 10%, from $14.8 million for the nine months ended September 30, 2020, to $16.3 million for the nine months ended September 30, 2021. The increase was due to a $1.0 million increase in professional services, primarily in legal expenses related to our Settlement Agreement and Release with Incyte and our Asset Purchase Agreement with Takeda, and a $1.5 million increase in personnel-related costs, primarily from increases in stock-based compensation expense, severance, and higher directors and officers liability insurance, partially offset by a $0.8 million decrease in rent expense related to the amendment of our facility lease in March 2021.

Interest and Other Income (expense), net. Interest and other income (expense), net decreased $0.8 million, or 70%, from $1.1 million for the nine months ended September 30, 2020 to $0.3 million for the nine months ended September 30, 2021. The decrease of $0.8 million was primarily due to $1.1 million in lower interest income generated from lower returns and lower balances on our investments, partially offset by a $0.4 million gain related to the remeasurement of our lease liability.

Liquidity and Capital Resources

As of September 30, 2021, we had cash and cash equivalents totaling $84.5 million. Our operations have been financed by net proceeds from the sale of shares of our capital stock and payments from the Company's collaboration and licensing agreements.

On October 18, 2021, we entered into an Asset Purchase Agreement 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 Convertible 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.

In August 2020, we filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission 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 September 30, 2021, $239.9 million of our common stock remained available for sale, of which $64.9 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.

For the nine months ended September 30, 2021, we sold 3,361,202 shares of our common stock under our ATM program at an average price per share of $3.02, for gross proceeds of $10.1 million, resulting in net proceeds of $9.9 million after deducting commissions and offering expenses.

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.

We believe that our existing cash and cash equivalents as of September 30, 2021 will be sufficient for us to meet our current operating plan for at least the twelve-month period following the filing of our September 30, 2021 Form 10-Q. 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. 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:

	Nine Months Ended September 30,	
	2021	2020
	(in thousands)	
Cash used in operating activities	$ (40,728)	$ (61,311)
Cash provided by investing activities	$ 7,892	$ 79,895
Cash provided by financing activities	$ 10,013	$ 41,561

Cash used in operating activities was $40.7 million for the nine months ended September 30, 2021, compared to $61.3 million for the nine months ended September 30, 2020. The decrease of $20.6 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 $7.9 million and $79.9 million for the nine months ended September 30, 2021 and 2020, respectively, and was related to proceeds from the sale and maturity of investments of $8 million and $137 million, respectively, partially offset by purchases of investments of $57.1 million in the nine month period ended September 30, 2020. For the nine months ended September 30, 2021 and 2020, the Company also purchased $0.1 million and $25,000 in property and equipment, respectively.

Cash provided by financing activities was $10.0 million and $41.6 million for the nine months ended September 30, 2021 and 2020, respectively. For the nine months ended September 30, 2021, we received $9.9 million in net proceeds from the sale and issuance of common stock related to our at-the-market offering program and $0.1 million in proceeds from the issuance of common stock upon the exercise of stock options and employee stock purchase plan purchases. For the nine months ended September 30, 2020, we received $33.5 million in net proceeds from the sale and issuance of common stock related to our public offering, $7.4 million in net proceeds from the sale and issuance of common stock related to our at-the-market offering program and $0.7 million in proceeds from the issuance of common stock upon the exercise of stock options and from employee stock plan purchases.

Contractual Obligations and Other Commitments

On March 8, 2021, we amended our facility lease to reduce our rentable area from approximately 54,000 square feet to approximately 34,000 square feet. The related reduction in rent was effective January 1, 2021. Please refer to Note 6 to our unaudited condensed consolidated financial statements appearing under Part I, Item 1 for a discussion of our amended lease.

There have been no other material changes to the contractual obligations during the three months ended September 30, 2021, as compared to those disclosed in our Annual Report on Form 10-K for the year ended December 31, 2020.

Off-Balance Sheet Arrangements

During 2020 and the nine months ended September 30, 2021, we did not have any off-balance sheet arrangements.

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 nine months ended September 30, 2021, 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, 2020.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures.

As of September 30, 2021, 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 September 30, 2021, 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 September 30, 2021, 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.
- We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- 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 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.

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 $90.1 million and $45.9 million for the year ended December 31, 2020, and the nine months ended September 30, 2021, respectively. As of September 30, 2021, we had an accumulated deficit of $422.1 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.

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

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. We expect that our existing cash, cash equivalents, and investments will be sufficient to enable us to meet our current operating plan for at least the next 12 months. However, our existing cash, cash equivalents and investments may prove to be insufficient for these activities. 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.

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 the Company's carryforward tax attributes may be subject to an annual limitation regarding their utilization against taxable income in future periods. As a result of the Company's IPO in 2014, the Company 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), the Company believes that an “ownership change” occurred during 2018, as well. Subsequent ownership changes since 2018 may subject the Company to annual limitations of its 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.*

On October 18, 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 telaglenastat, 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 with telaglenastat and INCB001158 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 telaglenastat, 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., Dracen Pharmaceuticals, 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 telaglenastat, 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 telaglenastat, 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 December 31, 2021. 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 Common Stock

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 pursuant to 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 or any other claim for which the U.S. federal courts have exclusive jurisdiction. 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. Our stockholders cannot waive compliance with the federal securities laws and the rules and regulations thereunder. 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, 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.

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 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	
10.1	Amended and Restated Severance Benefits Plan.					X
10.2^	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	
10.3†#	Asset Purchase Agreement, between Calithera Biosciences, Inc. and Millennium Pharmaceuticals, Inc., dated as of October 18, 2021.					X
10.4	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
104	The cover page from the Company's Quarterly Report on Form 10-Q for the three and nine months ended September 30, 2021, 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 September 30, 2021 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' 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: November 9, 2021

By: /s/ Susan M. Molineaux

Susan M. Molineaux, Ph.D.

President and Chief Executive Officer

(Principal Executive Officer)

Date: November 9, 2021

By: /s/ Stephanie Wong

Stephanie Wong

Chief Financial Officer and Secretary

(Principal Financial and Accounting Officer)

EXHIBIT 10.1

CALITHERA BIOSCIENCES, INC.

AMENDED AND RESTATED SEVERANCE BENEFIT PLAN

APPROVED BY THE COMPENSATION COMMITTEE OF THE BOARD OF DIRECTORS: AUGUST 28, 2017

AMENDED AND RESTATED BY THE COMPENSATION COMMITTEE OF THE BOARD OF DIRECTORS: AUGUST 21, 2021

A. INTRODUCTION.

The Calithera Biosciences, Inc. Severance Benefit Plan (the "***Plan***") is hereby established effective as set forth above. The purpose of the Plan is to provide for the payment of severance benefits to certain Eligible Employees (as defined below) in the event that such employees are subject to a Covered Termination. This Plan document is also the Summary Plan Description for the Plan.

For purposes of the Plan, the following terms are defined as follows:

i. "***Affiliate***" means any corporation (other than the Company) in an "unbroken chain of corporations" beginning with the Company, if each of the corporations other then the last corporation in the unbroken chain owns stock possessing fifty percent (50%) or more of the total combined voting power of all classes of stock in one of the other corporations in such chain.

ii. "***Base Salary***" means 1/12th of the Eligible Employee's annual base salary as in effect on the date of the Covered Termination, ignoring any reduction in base salary that forms the basis for Resignation for Good Reason.

iii. "***Board***" means the Board of Directors of the Company or the Compensation Committee of the Board of Directors of the Company.

i. "***Cause***" means one or more of the following, as determined by the Board in its sole discretion: (i) the Eligible Employee's conviction of or plea of *nolo contendere* to any felony or any crime involving moral turpitude or dishonesty; (ii) the Eligible Employee's gross misconduct in the performance of his or her duties which is injurious to the Company; (iii) failure by the Eligible Employee to substantially perform his or her material duties other than a failure resulting from the Eligible Employee's complete or partial incapacity due to physical or mental illness or impairment; (iv) the Eligible Employee's material breach of any agreement between the Eligible Employee and the Company concerning the terms and conditions of the Eligible Employee's employment with the Company; (v) the Eligible Employee's willful violation of a material Company employment policy (including, without limitation, any insider trading policy); or (vi) the Eligible Employee's commission of an act of fraud, breach of trust, or dishonesty including, without limitation, embezzlement, that results in material damage or harm to the business, financial condition, reputation or assets of the Company or any of its subsidiaries. Grounds for Cause pursuant to clause (iii) of this section shall not be deemed to have occurred until Company has first provided the Eligible Employee with written notice of the acts or omissions constituting the grounds for "Cause" under clause (iii) of this section and a cure period of thirty (30) days following the date of such notice.

ii. "***Change in Control***" means a "Change in Control" as defined in the Company's 2014 Equity Incentive Plan, as may be amended from time to time, provided that such transaction also qualifies

as “change in ownership of a corporation” or a “change in ownership of a substantial portion of a corporation’s assets” for purposes of Section 409A of the Code, if required for compliance with Section 409A of the Code.

iii. “***Closing***” means the initial closing of a Change in Control.

iv. “***COBRA***” means the Consolidated Omnibus Budget Reconciliation Act of 1985.

v. “***Code***” means the Internal Revenue Code of 1986, as amended.

vi. “***Company***” means Calithera Biosciences, Inc. or, following a Change in Control, the surviving entity resulting from the Change in Control, and any successor entity thereto.

vii. “***Covered Termination***” means a Qualifying Termination or a Qualifying CIC Termination

viii. “***Eligible Employee***” means an employee of the Company and its Subsidiaries specified by the Board as an eligible employee under the Plan and who otherwise meets the requirements to be eligible to receive Plan benefits as set forth in Section 2.

ix. “***Good Reason***” means (i) the assignment to an Eligible Employee of any duties, or the reduction of the Eligible Employee’s duties, either of which results in a material diminution of the Eligible Employee’s authority, duties, or responsibilities with the Company in effect immediately prior to such assignment or reduction, or the removal of the Eligible Employee from such position and responsibilities; (ii) a material reduction in the Eligible Employee’s base salary except in connection with a general reduction in salary applicable to all of the Company’s executive officers other than in connection with or following a Change in Control; (iii) a relocation of the Eligible Employee’s principal place of employment by more than thirty (30) miles; or (iv) any material breach by the Company of any material provision of the Eligible Employee’s employment agreement with the Company, provided and only if such change, reduction or relocation is effected without the Eligible Employee’s written consent. In order for the Eligible Employee to resign for Good Reason, the Eligible Employee must provide advance notice of such resignation to the Company within ninety (90) days following the initial existence of the action or event giving rise to Good Reason. The notice must specify an effective date of termination that is not less than thirty (30) days, nor more than sixty (60) days, after the date of the written notice, and the Eligible Employee agrees that should the Company remedy the basis for such resignation prior to the termination date specified in the written notice, then the Eligible Employee may not resign for Good Reason. The Company may relieve the Eligible Employee of some or all of his or her duties, responsibilities and authority during any notice period, and such relief shall not serve as a basis for Eligible Employee to claim Good Reason, provided that the Company reinstates such duties, responsibilities, and authority not later than the last day of such notice period.

x. ***“Individual Severance Arrangement”*** means any individual employment offer letter, contract or agreement that an Eligible Employee has with the Company providing for severance benefits to an Eligible Employee or any other severance arrangement between the Eligible Employee and the Company.

xi. “***Plan Administrator***” means the Board prior to the Closing and such person, group or entity as the Board may designate upon and following the Closing.

xii. “***Protection Period***” means the period of time commencing immediately prior to the Closing and continuing through the date that is twelve (12) months following the Closing.

xiii. ***"Qualifying Termination"*** means a termination of the Eligible Employee's employment by (i) the Company other than for Cause (and not by reason of death or disability), or (ii) the Eligible Employee for Good Reason, in either case other than during the Protection Period.

xiv. ***"Qualifying CIC Termination"*** means a termination of the Eligible Employee's employment by (i) the Company other than for Cause (and not by reason of death or disability), or (ii) the Eligible Employee for Good Reason, in either case during the Protection Period. For such purposes, if the events giving rise to an Eligible Employee's right to resign for Good Reason arise within the Protection Period, and the employee's resignation occurs not later than thirty (30) days after the expiration of the Cure Period (as defined above), such termination shall be a Qualifying CIC Termination even if the termination occurs following the Protection Period.

xv. "***Subsidiary***" means, with respect to the Company, (i) any corporation of which more than fifty percent (50%) of the outstanding capital stock having ordinary voting power to elect a majority of the board of directors of such corporation (irrespective of whether, at the time, stock of any other class or classes of such corporation shall have or might have voting power by reason of the happening of any contingency) is at the time, directly or indirectly, owned by the Company, and (ii) any partnership, limited liability company or other entity in which the Company has a direct or indirect interest (whether in the form of voting or participation in profits or capital contribution) of more than fifty percent (50%).

xvi. "***Target Bonus***" shall mean the Eligible Employee's target bonus opportunity, if any, established by the Board and expressed as a percentage of annual base salary, under the Company's annual cash incentive plan or program under which such Eligible Employee is eligible to participate, as in effect (i) immediately prior to the Change in Control or (ii) immediately prior to the employee's Covered Termination, whichever of (i) or (ii) is greater.

B.ELIGIBILITY FOR BENEFITS.

i. **Eligible Employee**. An employee of the Company or a Subsidiary is eligible to participate in the Plan if (i) such employee is the Company's Chief Executive Officer, is at the Senior Vice President level or above, is at the Vice President level or is designated in writing as a participant by the Board; (ii) such employee's employment with the Company and its Subsidiaries terminates due to a Covered Termination; and (iii) such employee meets the other Plan eligibility requirements set forth in this Section 2.

ii. **Release Requirement.** In order to be eligible to receive payments and benefits under the Plan, the employee also must execute a general waiver and release in substantially the form provided by the Company (the "***Release***"), within the applicable time period set forth therein, and such Release must become effective in accordance with its terms (the date of such effectiveness, the "***Release Effective Date***"), which shall in no event be later than sixty (60) days following the date of the applicable Covered Termination. The Company, in its sole discretion, will determine the form of the Release so that to complies with applicable law and the specific terms of the Covered Termination, which may be incorporated into a termination agreement or other agreement with the employee.

iii. **No Duplicative Benefits Provided Under Plan.** This Plan supersedes the terms of any Individual Severance Arrangement.

iv. **Exceptions to Benefit Entitlement.** An employee who otherwise is an Eligible Employee will not receive benefits under the Plan in the following circumstances, as determined by the Plan Administrator in its sole discretion:

1. The employee voluntarily terminates employment with the Company and its Subsidiaries without Good Reason, or terminates employment due to the employee's death.

2. The employee voluntarily terminates employment with the Company and its Subsidiaries in order to accept employment with another entity that is wholly or partly owned (directly or indirectly) by the Company or an Affiliate.

3. The employee's employment is transferred by the Company to an Affiliate of the Company and such transfer does not give rise to the employee's right to resign for Good Reason.

4. The employee is rehired by the Company or an Affiliate and recommences employment at any time that benefits under the Plan remain unpaid (but only as to the unpaid portion thereof).

v. Each Eligible Employee must sign and return the Designation Letter, in substantially the form attached hereto as **Exhibit A**, to the Company within ten (10) days after being provided such Designation Letter to agree to the terms and conditions of the Plan.

a.Amount of Benefit.

i. Severance Benefit. Upon a Covered Termination, the Eligible Employee shall be eligible to receive the following severance benefits.

1. Cash Severance Benefit. The Eligible Employee shall receive a payment equal to the sum of (A) a number of months (such number of months, the "***Severance Term***") multiplied by the Eligible Employee's Base Salary; and (B) one-twelfth (1/12) of the Eligible Employee's Target Bonus multiplied by the Severance Term, which either (i) in a Qualifying CIC Termination, shall be a lump sum payment provided within ten (10) days following the Release Effective Date or (ii) in a Qualifying Termination, shall be paid in equal installments on the Company's normal payroll schedule over the number of months equal to the Severance Term immediately following the date of the Qualified Termination with the first payment being made on the first regular payroll date following the Release Effective Date:

Title	Qualifying Termination: Severance Term	Qualifying CIC Termination: Severance Term
CEO	12	18
Senior Vice Presidents	12	12
Vice Presidents	9	9

2. Continued Group Health Plan Benefits.

a. If the Eligible Employee timely elects continued group health plan continuation coverage under COBRA, the Company shall pay a portion of the Eligible Employee's premiums on behalf of the Eligible Employee for the Eligible Employee's continued coverage under the

Company's group health plans, including coverage for the Eligible Employee's eligible dependents, for a number of months equal to the applicable Severance Term or until such earlier date on which the Eligible Employee becomes eligible for health coverage from another employer (the "***COBRA Payment Period***"). The amount of this portion will be the same portion of the premium cost as was borne by the Company under the level of coverage selected by the Eligible Employee and in effect at the time of the Covered Termination. Upon the conclusion of such period of insurance premium payments made by the Company, or the provision of coverage under a self-funded group health plan, the Eligible Employee will be responsible for the entire payment of premiums (or payment for the cost of coverage) required under COBRA for the duration of the Eligible Employee's eligible COBRA coverage period. For purposes of this Section, (i) references to COBRA shall be deemed to refer also to analogous provisions of state law and (ii) any applicable insurance premiums that are paid by the Company shall not include any amounts payable by the Eligible Employee under an Internal Revenue Code Section 125 health care reimbursement plan, which amounts, if any, are the Eligible Employee's sole responsibility.

b. Notwithstanding the foregoing, if the Eligible Employee timely elects continued group health plan continuation coverage under COBRA and at any time thereafter the Company determines, in its sole discretion, that it cannot provide the COBRA premium benefits without potentially incurring financial costs or penalties under applicable law (including, without limitation, Section 2716 of the Public Health Service Act), then in lieu of paying the employer portion of the COBRA premiums on the Eligible Employee's behalf, the Company will instead pay the Eligible Employee on the last day of each remaining month of the COBRA Payment Period a fully taxable cash payment equal to the employer portion of the COBRA premium for that month, subject to applicable tax withholding (such amount, the "***Special Severance Payment***"). Such Special Severance Payment shall end upon expiration of the COBRA Payment Period

3. *Equity Vesting.* If the Covered Termination is a Qualified CIC Termination, then all unvested equity awards held by the Eligible Employee as of the date of the Qualified CIC Termination shall not terminate prior to the Release Effective Date but rather shall vest as of the Release Effective Date; provided, however, that if the Release is revoked, such unvested equity awards shall terminate as of the date of such revocation. For the avoidance of doubt, such unvested equity awards shall not vest under the terms of the Plan in connection with a Qualified Termination.

ii. **Additional Benefits.** Notwithstanding the foregoing, the Company may, in its sole discretion, provide benefits to individuals who are not Eligible Employees ("***Non-Eligible Employees***") chosen by the Board, in its sole discretion, and the provision of any such benefits to a Non-Eligible Employee shall in no way obligate the Company to provide such benefits to any other Non-Eligible Employee, even if similarly situated. If benefits under the Plan are provided to a Non-Eligible Employee, references in the Plan to "Eligible Employee" (and similar references) shall be deemed to refer to such Non-Eligible Employee.

iii. **Certain Reductions.** The Company, in its sole discretion, shall have the authority to reduce an Eligible Employee's severance benefits, in whole or in part, by any other severance benefits, pay and benefits provided during a period following written notice of a plant closing or mass layoff, pay and benefits in lieu of other statutory notice periods, or other similar benefits payable to the Eligible Employee by the Company or an Affiliate that become payable in connection with the Eligible Employee's termination of employment pursuant to (i) any applicable US or non-US federal, state, local legal requirement, including, without limitation, the Worker Adjustment and Retraining Notification Act or any other similar state law, or (i) any policy or practice of the Company and its Subsidiaries providing for the Eligible Employee to remain on the payroll for a limited period of time after being given notice of the termination of the Eligible Employee's employment, and the Plan Administrator shall so construe and implement the terms of the Plan. Any such reductions that the Company determines to make pursuant to this Section 3(c)

shall be made such that any benefit under the Plan shall be reduced solely by any similar type of benefit under such legal requirement, agreement, policy or practice (*i.e.*, any cash severance benefits under the Plan shall be reduced solely by any cash payments or severance benefits under such legal requirement, agreement, policy or practice, and any continued insurance benefits under the Plan shall be reduced solely by any continued insurance benefits under such legal requirement, agreement, policy or practice). The Company's decision to apply such reductions to the severance benefits of one Eligible Employee and the amount of such reductions shall in no way obligate the Company to apply the same reductions in the same amounts to the severance benefits of any other Eligible Employee, even if similarly situated. In the Company's sole discretion, such reductions may be applied on a retroactive basis, with severance benefits previously paid being re-characterized as payments pursuant to the Company's statutory obligation.

B.RETURN OF COMPANY PROPERTY.

An Eligible Employee will not be entitled to any severance benefit under the Plan unless and until the Eligible Employee returns all Company Property. For this purpose, "Company Property" means all Company documents (and all copies thereof) and other Company property which the Eligible Employee had in his or her possession at any time, including, but not limited to, Company files, notes, drawings, records, plans, forecasts, reports, studies, analyses, proposals, agreements, financial information, research and development information, sales and marketing information, operational and personnel information, specifications, code, software, databases, computer-recorded information, tangible property and equipment (including, but not limited to, computers, facsimile machines, mobile telephones, servers), credit cards, entry cards, identification badges and keys; and any materials of any kind which contain or embody any proprietary or confidential information of the Company (and all reproductions thereof in whole or in part).

C.TAXATION AND OFFSETS.

(a) General. Severance payments under the Plan will be subject to applicable withholding for federal, state and local taxes. If an Eligible Employee is indebted to the Company on his or her termination date, the Company reserves the right to offset any severance payments under the Plan by the amount of such indebtedness to the maximum extent permitted by applicable law. All severance benefits provided under the Plan are intended to satisfy the requirements for an exemption from application of Section 409A of the Code to the maximum extent that an exemption is available and any ambiguities herein shall be interpreted accordingly; provided, however, that to the extent such an exemption is not available, the severance benefits provided under the Plan are intended to comply with the requirements of Section 409A to the extent necessary to avoid adverse personal tax consequences and any ambiguities herein shall be interpreted accordingly. Severance benefits provided under the Plan will not be included as compensation under any employee benefit plan of the Company or any of its affiliates unless expressly required under the terms thereof.

(b) Section 409A. Notwithstanding anything to the contrary set forth herein, any payments and benefits provid under the Plan that constitute "deferred compensation" within the meaning of Section 409A of the Code and the regulations and other guidance thereunder and any state law of similar effect (collectively "***Section 409A***") shall not commence in connection with an Eligible Employee's termination of employment unless and until the Eligible Employee has also incurred a "separation from service," as such term is defined in Treasury Regulations Section 1.409A-1(h) ("***Separation from Service***"), unless the Company reasonably determines that such amounts may be provided to the Eligible Employee without causing the Eligible Employee to incur the adverse personal tax consequences under Section 409A.

It is intended that (i) each installment of any benefits payable under the Plan to an Eligible Employee be regarded as a separate "payment" for purposes of Treasury Regulations Section 1.409A-2(b)(2)(i), (ii) all payments of any such benefits under the Plan satisfy, to the greatest extent possible, the

exemptions from the application of Section 409A provided under Treasury Regulations Sections 1.409A-1(b)(4) and 1.409A-1(b)(9)(iii), and (iii) any such benefits consisting of COBRA premiums also satisfy, to the greatest extent possible, the exemption from the application of Section 409A provided under Treasury Regulations Section 1.409A-1(b)(9)(v). However, if the Company determines that any such benefits payable under the Plan constitute "deferred compensation" under Section 409A and the Eligible Employee is a "specified employee" of the Company, as such term is defined in Section 409A(a)(2)(B)(i), then, solely to the extent necessary to avoid the imposition of the adverse personal tax consequences under Section 409A, (A) the timing of such benefit payments shall be delayed until the earlier of (1) the date that is six (6) months and one (1) day after the Eligible Employee's Separation from Service and (2) the date of the Eligible Employee's death (such applicable date, the "***Delayed Initial Payment Date***"), and (B) the Company shall (1) pay the Eligible Employee a lump sum amount equal to the sum of the benefit payments that the Eligible Employee would otherwise have received through the Delayed Initial Payment Date if the commencement of the payment of the benefits had not been delayed pursuant to this paragraph and (2) commence paying the balance, if any, of the benefits in accordance with the applicable payment schedule.

In no event shall payment of any benefits under the Plan be made prior to an Eligible Employee's termination date or prior to the effective date of the Release. If the Company determines that any payments or benefits provided under the Plan constitute "deferred compensation" under Section 409A, and the Eligible Employee's Separation from Service occurs at a time during the calendar year when the Release could become effective in the calendar year following the calendar year in which the Eligible Employee's Separation from Service occurs, then regardless of when the Release is returned to the Company and becomes effective, the Release will not be deemed effective any earlier than the first day of that following calendar year. If the Company determines that any payments or benefits provided under the Plan constitute "deferred compensation" under Section 409A, then except to the extent that payments may be delayed until the Delayed Initial Payment Date pursuant to the preceding paragraph, on the first regular payroll date following the effective date of an Eligible Employee's Release, the Company shall (1) pay the Eligible Employee a lump sum amount equal to the sum of the benefit payments that the Eligible Employee would otherwise have received through such payroll date but for the delay in payment related to the effectiveness of the Release and (2) commence paying the balance, if any, of the benefits in accordance with the applicable payment schedule.

(c) Parachute Payments. In the event that any of the severance payments and other benefits provided by this Plan or otherwise payable to an Eligible Employee (a) constitute "parachute payments" within the meaning of Section 280G of the Code, and (b) but for this Section, would be subject to the excise tax imposed by Section 4999 of the Code ("***Excise Tax***"), the Eligible Employee's severance payments and benefits under this Plan or otherwise shall be payable either in full or in such lesser amount which would result in no portion of such severance payments or benefits being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local income and employment taxes and the Excise Tax, results in the receipt by the Eligible Employee, on an after-tax basis, of the greatest amount of severance payments and benefits under this Plan or otherwise, notwithstanding that all or some portion of such severance payments or benefits may be taxable under Section 4999 of the Code. Any reduction in the severance payments and benefits required by this Section shall be made in the following order: (i) reduction of cash payments; (ii) reduction of accelerated vesting of equity awards other than stock options; (iii) reduction of accelerated vesting of stock options; and (iv) reduction of other benefits paid or provided to the Eligible Employee.

The calculations in this Section will be performed by the professional firm engaged by the Company for general tax purposes as of the day prior to the date of the event that might reasonably be anticipated to result in severance payments and benefits that would otherwise be subject to the Excise Tax. If the tax firm so engaged by the Company is serving as accountant or auditor for the acquiring company, the Company shall appoint a nationally recognized tax firm to make the determinations required by this

Section. The Company shall bear all expenses with respect to the determinations by such firm required to be made by this Section. The Company and the Eligible Employee shall furnish such tax firm such information and documents as the tax firm may reasonably request in order to make its required determination. The tax firm will provide its calculations, together with detailed supporting documentation, to the Company and the Eligible Employee as soon as practicable following its engagement. Any good faith determinations of the tax firm made hereunder shall be final, binding and conclusive upon the Company and the Eligible Employee. However, the Eligible Employee shall have the final authority to make any good faith determination(s) associated with the assumptions used by the tax firm in providing its calculations, and such good faith determination by the Eligible Employee shall be binding on the Company.

As a result of the uncertainty in the application of Sections 409A, 280G or 4999 of the Code at the time of the initial determination by the professional tax firm described in this Section, it is possible that the Internal Revenue Service (the "***IRS***") or other agency will claim that an Excise Tax greater than that amount, if any, determined by such professional firm for the purposes of this Section is due (the "***Additional Excise Tax***"). The Eligible Employee shall notify the Company in writing of any claim by the IRS or other agency that, if successful, would require payment of Additional Excise Tax. The Eligible Employee and the Company shall each reasonably cooperate with the other in connection with any administrative or judicial proceedings concerning the existence or amount of liability for Excise Tax with respect to payments made or due to the Eligible Employee. The Company shall pay all reasonable fees, expenses and penalties of the Eligible Employee relating to a claim by the IRS or other agency. In the event it is finally determined that a further reduction would have been required under this Section to place the Eligible Employee in a better after-tax position, the Eligible Employee shall repay the Company such amount within thirty (30) days thereof in order to effect such result.

D.RIGHT TO INTERPRET AND ADMINISTER PLAN; AMENDMENT AND TERMINATION.

i. Interpretation and Administration. Prior to the Closing, the Board shall be the Plan Administrator and shall have the exclusive discretion and authority to establish rules, forms, and procedures for the administration of the Plan and to construe and interpret the Plan and to decide any and all questions of fact, interpretation, definition, computation or administration arising in connection with the operation of the Plan, including, but not limited to, the eligibility to participate in the Plan and amount of benefits paid under the Plan and the resolution of disputes under the Plan. The rules, interpretations, computations and other actions of the Board shall be binding and conclusive on all persons. Upon and after the Closing, the Plan will be interpreted and administered in good faith by the Plan Administrator. All actions taken by the Plan Administrator in interpreting the terms of the Plan and administering the Plan upon and after the Closing will be final and binding on all Eligible Employees.

ii. Amendment or Termination. The Plan Administrator reserves the right to amend or terminate this Plan at any time; provided, however, that no such amendment or termination will apply to any Participant who would be adversely affected by such amendment or termination unless such Participant consents in writing to such amendment or termination. Any action amending or terminating the Plan or any Designation Letter will be in writing and executed by a duly authorized officer of the Company.

E.NO IMPLIED EMPLOYMENT CONTRACT.

The Plan shall not be deemed (i) to give any employee or other person any right to be retained in the employ of the Company or (ii) to interfere with the right of the Company to discharge any employee or other person at any time, with or without cause, which right is hereby reserved.

f.Legal Construction.

This Plan is intended to be governed by and shall be construed in accordance with the Employee Retirement Income Security Act of 1974 ("***ERISA***") and, to the extent not preempted by ERISA, the laws of the State of California.

g.Claims, Inquiries and Appeals.

i. Applications for Benefits and Inquiries. Any application for benefits, inquiries about the Plan or inquiries about present or future rights under the Plan must be submitted to the Plan Administrator in writing by an applicant (or his or her authorized representative). The Plan Administrator is:

Calithera Biosciences, Inc.
Board of Directors
343 Oyster Point Blvd, #200
South San Francisco, CA 94080

ii. Denial of Claims. In the event that any application for benefits is denied in whole or in part, the Plan Administrator must provide the applicant with written or electronic notice of the denial of the application, and of the applicant's right to review the denial. Any electronic notice will comply with the regulations of the U.S. Department of Labor. The notice of denial will be set forth in a manner designed to be understood by the applicant and will include the following:

1. the specific reason or reasons for the denial;

2. references to the specific Plan provisions upon which the denial is based;

3. a description of any additional information or material that the Plan Administrator needs to complete the review and an explanation of why such information or material is necessary; and

4. an explanation of the Plan's review procedures and the time limits applicable to such procedures, including a statement of the applicant's right to bring a civil action under Section 502(a) of ERISA following a denial on review of the claim, as described in Section 10(d) below.

This notice of denial will be given to the applicant within ninety (90) days after the Plan Administrator receives the application, unless special circumstances require an extension of time, in which case, the Plan Administrator has up to an additional ninety (90) days for processing the application. If an extension of time for processing is required, written notice of the extension will be furnished to the applicant before the end of the initial ninety (90) day period.

This notice of extension will describe the special circumstances necessitating the additional time and the date by which the Plan Administrator is to render its decision on the application.

iii. Request for a Review. Any person (or that person's authorized representative) for whom an application for benefits is denied, in whole or in part, may appeal the denial by submitting a request for a review to the Plan Administrator within sixty (60) days after the application is denied. A request for a review shall be in writing and shall be addressed to:

Calithera Biosciences, Inc.

A request for review must set forth all of the grounds on which it is based, all facts in support of the request and any other matters that the applicant feels are pertinent. The applicant (or his or her representative) shall have the opportunity to submit (or the Plan Administrator may require the applicant to submit) written comments, documents, records, and other information relating to his or her claim. The applicant (or his or her representative) shall be provided, upon request and free of charge, reasonable access to, and copies of, all documents, records and other information relevant to his or her claim. The review shall take into account all comments, documents, records and other information submitted by the applicant (or his or her representative) relating to the claim, without regard to whether such information was submitted or considered in the initial benefit determination.

iv. Decision on Review. The Plan Administrator will act on each request for review within sixty (60) days after receipt of the request, unless special circumstances require an extension of time (not to exceed an additional sixty (60) days), for processing the request for a review. If an extension for review is required, written notice of the extension will be furnished to the applicant within the initial sixty (60) day period. This notice of extension will describe the special circumstances necessitating the additional time and the date by which the Plan Administrator is to render its decision on the review. The Plan Administrator will give prompt, written or electronic notice of its decision to the applicant. Any electronic notice will comply with the regulations of the U.S. Department of Labor. In the event that the Plan Administrator confirms the denial of the application for benefits in whole or in part, the notice will set forth, in a manner calculated to be understood by the applicant, the following:

1. the specific reason or reasons for the denial;

2. references to the specific Plan provisions upon which the denial is based;

3. a statement that the applicant is entitled to receive, upon request and free of charge, reasonable access to, and copies of, all documents, records and other information relevant to his or her claim; and

4. a statement of the applicant's right to bring a civil action under Section 502(a) of ERISA.

v. Rules and Procedures. The Plan Administrator will establish rules and procedures, consistent with the Plan and with ERISA, as necessary and appropriate in carrying out its responsibilities in reviewing benefit claims. The Plan Administrator may require an applicant who wishes to submit additional information in connection with an appeal from the denial of benefits to do so at the applicant's own expense.

vi. Exhaustion of Remedies. No legal action for benefits under the Plan may be brought until the applicant (i) has submitted a written application for benefits in accordance with the procedures described by Section 9(a) above, (ii) has been notified by the Plan Administrator that the application is denied, (iii) has filed a written request for a review of the application in accordance with the appeal procedure described in Section 9(c) above, and (iv) has been notified that the Plan Administrator has denied the appeal. Notwithstanding the foregoing, if the Plan Administrator does not respond to an Eligible Employee's claim or appeal within the relevant time limits specified in this Section 9, the Eligible Employee may bring legal action for benefits under the Plan pursuant to Section 502(a) of ERISA.

H.BASIS OF PAYMENTS TO AND FROM PLAN.

The Plan shall be unfunded, and all cash payments under the Plan shall be paid only from the general assets of the Company.

I.OTHER PLAN INFORMATION.

i. Employer and Plan Identification Numbers. The Employer Identification Number assigned to the Company (which is the "Plan Sponsor" as that term is used in ERISA) by the Internal Revenue Service is 27-2366329. The Plan Number assigned to the Plan by the Plan Sponsor pursuant to the instructions of the Internal Revenue Service is 500.

ii. Ending Date for Plan's Fiscal Year. The date of the end of the fiscal year for the purpose of maintaining the Plan's records is December 31.

iii. Agent for the Service of Legal Process. The agent for the service of legal process with respect to the Plan is:

Calithera Biosciences, Inc.
343 Oyster Point Blvd, #200
South San Francisco, CA 94080

In addition, service of legal process may be made upon the Plan Administrator.

iv. Plan Sponsor. The "Plan Sponsor" is:

Calithera Biosciences, Inc.
343 Oyster Point Blvd, #200
South San Francisco, CA 94080
(650) 870-1000

v. Plan Administrator. The Plan Administrator's contact information is:

Calithera Biosciences, Inc.
Board of Directors
343 Oyster Point Blvd, #200
South San Francisco, CA 94080
(650) 870-1000

The Plan Administrator is the named fiduciary charged with the responsibility for administering the Plan.

J.STATEMENT OF ERISA RIGHTS.

Participants in this Plan (which is a welfare benefit plan sponsored by Calithera Biosciences, Inc.) are entitled to certain rights and protections under ERISA. If you are an Eligible Employee, you are considered a participant in the Plan and, under ERISA, you are entitled to:

i. Receive Information About Your Plan and Benefits.

1. Examine, without charge, at the Plan Administrator's office and at other specified locations, such as worksites, all documents governing the Plan and a copy of the latest annual

report (Form 5500 Series), if applicable, filed by the Plan with the U.S. Department of Labor and available at the Public Disclosure Room of the Employee Benefits Security Administration;

2. Obtain, upon written request to the Plan Administrator, copies of documents governing the operation of the Plan and copies of the latest annual report (Form 5500 Series), if applicable, and an updated (as necessary) Summary Plan Description. The Administrator may make a reasonable charge for the copies; and

3. Receive a summary of the Plan's annual financial report, if applicable. The Plan Administrator is required by law to furnish each Eligible Employee with a copy of this summary annual report.

ii. Prudent Actions by Plan Fiduciaries. In addition to creating rights for Plan Eligible Employees, ERISA imposes duties upon the people who are responsible for the operation of the employee benefit plan. The people who operate the Plan, called "fiduciaries" of the Plan, have a duty to do so prudently and in the interest of you and other Eligible Employees and beneficiaries. No one, including your employer, your union or any other person, may fire you or otherwise discriminate against you in any way to prevent you from obtaining a Plan benefit or exercising your rights under ERISA.

iii. Enforce Your Rights. If your claim for a Plan benefit is denied or ignored, in whole or in part, you have a right to know why this was done, to obtain copies of documents relating to the decision without charge, and to appeal any denial, all within certain time schedules.

Under ERISA, there are steps you can take to enforce the above rights. For instance, if you request a copy of Plan documents or the latest annual report from the Plan, if applicable, and do not receive them within thirty (30) days, you may file suit in a Federal court. In such a case, the court may require the Plan Administrator to provide the materials and pay you up to $110 a day until you receive the materials, unless the materials were not sent because of reasons beyond the control of the Plan Administrator.

If you have a claim for benefits which is denied or ignored, in whole or in part, you may file suit in a state or Federal court.

If you are discriminated against for asserting your rights, you may seek assistance from the U.S. Department of Labor, or you may file suit in a Federal court. The court will decide who should pay court costs and legal fees. If you are successful, the court may order the person you have sued to pay these costs and fees. If you lose, the court may order you to pay these costs and fees, for example, if it finds your claim is frivolous.

iv. Assistance with Your Questions. If you have any questions about the Plan, you should contact the Plan Administrator. If you have any questions about this statement or about your rights under ERISA, or if you need assistance in obtaining documents from the Plan Administrator, you should contact the nearest office of the Employee Benefits Security Administration, U.S. Department of Labor, listed in your telephone directory or the Division of Technical Assistance and Inquiries, Employee Benefits Security Administration, U.S. Department of Labor, 200 Constitution Avenue N.W., Washington, D.C. 20210. You may also obtain certain publications about your rights and responsibilities under ERISA by calling the publications hotline of the Employee Benefits Security Administration.

EXHIBIT A

CALITHERA BIOSCIENCES, INC.

SEVERANCE BENEFIT PLAN
DESIGNATION AS A PARTICIPANT

To:

Date:

Calithera Biosciences, Inc. (the "***Company***") has adopted the Calithera Biosciences, Inc. Severance Benefit Plan (the "***Plan***"). The Company is providing you this letter to inform you that you have been designated as a Participant in the Plan. A copy of the Plan document is attached to this letter. The terms and conditions of your participation in the Plan are as set forth in the Plan and this letter, which together constitute the Summary Plan Description for the Plan.

By accepting participation, you represent that you have either consulted your personal tax or financial planning advisor about the tax consequences of your participation in the Plan, or you have knowingly declined to do so. In addition, you agree that by accepting participation in the Plan the severance benefits set forth in your [offer letter] with the Company dated [_____] (the "***Prior Agreement***") shall automatically become null and void and of no further force and effect and you shall have no further rights under the Prior Agreement, effective as of the date set forth above.

Please return to the Company's Vice President Finance a copy of this letter signed by you and retain a copy of this letter, along with the Plan document, for your records. To be eligible to participate in the Plan, you must sign this letter within 10 days after being provided a copy.

CALITHERA BIOSCIENCES, INC.:

(Signature)

By:

Title:

PARTICIPANT:

(Signature)

By:

Date:

255060741 v3

CONFIDENTIAL **EXECUTION VERSION**

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

ASSET PURCHASE AGREEMENT

between

Millennium Pharmaceuticals, Inc.

and

Calithera Biosciences, Inc.

Dated as of October 18, 2021

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ASSET PURCHASE AGREEMENT

This Asset Purchase Agreement (this "**Agreement**") is made and entered into as of October 18, 2021, between Millennium Pharmaceuticals, Inc., a Delaware corporation ("**Seller**"), and Calithera Biosciences, Inc., a Delaware corporation ("**Buyer**"). Buyer and Seller are sometimes referred to herein individually as a "**Party**" and collectively as the "**Parties**".

RECITALS

WHEREAS, Seller owns or controls certain technology and intellectual property related to Seller's small molecule programs internally coded by Seller as TAK-228 and TAK-659; and

WHEREAS, Seller desires to sell to Buyer, or to license to Buyer, and Buyer desires to purchase from Seller, or license from Seller, certain assets of Seller used in or relating to Seller's TAK-228 and TAK-659 programs, and Buyer is willing to assume certain liabilities of Seller relating to such TAK-228 and TAK-659 programs, all upon the terms and conditions set forth herein.

NOW, THEREFORE, in consideration of the premises and the mutual covenants, representations and warranties herein contained, and for other good and valuable consideration, the receipt and sufficiency of which are hereby mutually acknowledged, the Parties hereby agree as follows:

ARTICLE 1.
DEFINITIONS

1.1 **Defined Terms**. As used in this Agreement, the following defined terms shall have the meanings specified below:

"**Additional Active**" means one (1) or more active pharmaceutical or biological ingredients for which no earn-out payments would be due hereunder if such ingredient(s) were sold separately from a Product.

"**Affiliate**" means, with respect to any Person, any other Person that controls, is controlled by or is under common control with such Person, for as long as such control exists. For purposes of this definition, "control" means the direct or indirect ownership of more than fifty percent (50%) of the voting or economic interest of a Person, or the power, whether pursuant to contract, ownership of securities or otherwise, to direct the management and policies of a Person. For clarity, once a Person ceases to be an Affiliate of a Party, then, without any further action, such Person shall no longer be considered an Affiliate of such Party for purposes of this Agreement.

"**Ancillary Agreements**" means, collectively, the Bill of Sale, the Patent Assignment Agreement, the Equity Agreement and such other agreements as may be executed in connection with the transactions contemplated by this Agreement.

"**Annual Net Sales**" means, with respect to a Product, the cumulative worldwide Net Sales of such Product in any Calendar Year.

"**Assigned Agreements**" means, subject to Section 3.9, the agreements set forth on Schedule 1.1(f).

"**Assigned Intellectual Property**" means the Assigned Patent Rights and the Assigned Know-How, including Seller's interest in Transaction IP that is solely related to either or both Programs.

"**Assigned Know-How**" means Know-How that is: (a) owned by Seller or any of its Affiliates (i) as of the Closing Date or (ii) on or after the Closing Date and (A) included in the Transaction IP or (B) owned pursuant to a Non-Assignable Contract or Related Agreement, in each case (A) and (B) pursuant to Section 4.3, (b) necessary to research and develop, make, have made, use, sell, offer for sale, and import any Product in the Field in the Territory, and (c) solely related to either or both Programs, as applicable. The Assigned Know-How as of the Closing Date is set forth on Schedule 1.1(g). For clarity, Know-How relating to a Program Molecule in combination with a Takeda Compound is explicitly excluded from Assigned Know-How.

"**Assigned Patent Rights**" means (x) Patent Rights that are: (a) owned by Seller or any of its Affiliates (i) as of the Closing Date or (ii) on or after the Closing Date and (A) included in the Transaction IP or (B) owned pursuant to a Non-Assignable Contract or Related Agreement, in each case (A) and (B) pursuant to Section 4.3, (b) necessary to research and develop, make, have made, use, sell, offer for sale, and import any Product in the Field in the Territory, and (c) solely related to either or both Programs, as applicable, and (y) Patent Rights that claim priority to the Patent Rights in the preceding clause (x). The Assigned Patent Rights as of the Closing Date are set forth on Schedule 1.1(h) – Part 1. For clarity, Assigned Patent Rights do not include any Patent Rights relating to a Program Molecule in combination with a Takeda Compound.

"**Bill of Sale**" means the bill of sale to be executed and delivered at Closing, substantially in the form of Exhibit A, selling, assigning, transferring, conveying and delivering the Acquired Assets.

"**Business Day**" means any day that is not: (a) a Saturday or a Sunday or (b) any day that is a legal holiday under the applicable Laws of the United States or Japan or that is a day on which banking institutions in New York City, New York, or Tokyo, Japan, are authorized or required by applicable Laws or other governmental action to close.

"**Calendar Quarter**" means the period beginning on the Closing Date and ending on the last day of the calendar quarter in which the Closing Date falls, and thereafter each successive period of three (3) consecutive calendar months ending on March 31, June 30, September 30 and December 31; *provided*, *that*, the final Calendar Quarter shall end on the last day of the Term.

"**Calendar Year**" means the period beginning on the Closing Date and ending on December 31 of the calendar year in which the Closing Date falls, and thereafter each successive period of twelve (12) months commencing on January 1 and ending on December 31; *provided*, *that*, the final Calendar Year shall end on the last day of the Term.

"**CDA**" means the Confidential Disclosure Agreement dated as of March 26, 2021 (the "**CDA Effective Date**") by and between Buyer and Takeda Pharmaceuticals U.S.A., Inc.

"**Change of Control**" means any of the following: (a) the acquisition by a Third Party, directly or indirectly, of the beneficial ownership of any voting security of a Party, or increase in the percentage ownership of a Third Party in the voting securities of a Party through stock redemption, cancellation or other recapitalization, where immediately after such acquisition or increase such Third Party is, directly or indirectly, the beneficial owner of voting securities representing more than fifty percent (50%) of the total voting power of all of the then-outstanding voting securities of such Party; (b) the consummation of a merger, consolidation, recapitalization, reorganization, amalgamation, arrangement, share exchange, tender or exchange offer, private purchase, business combination or other transaction of a Party, other than any such transaction which would result in an Affiliate of a Party, immediately prior to such transaction, owning fifty percent (50%) or more of the outstanding securities of the surviving entity (or its parent entity) immediately following such transaction; or (c) the sale or disposition by such Party of all or a substantial

portion of such Party's assets or all or substantially all of such Party's assets which relate to this Agreement to a Third Party, other than to an Affiliate of such Party.

"**Code**" means the Internal Revenue Code of 1986, as amended.

"**Combination Product**" means any (a) product that includes a Program Molecule and one (1) or more Additional Actives or (b) Product sold with one (1) or more other product(s) containing or comprising one (1) or more Additional Actives for a single invoice price.

"**Commercially Reasonable Efforts**" means with respect to development or commercialization activities that Buyer performs pursuant to this Agreement, the level of effort that [***].

"**Contracts**" means any and all binding commitments, contracts, purchase orders, licenses, or other agreements, whether written or oral.

"**Control**" means, with respect to any Know-How or Patent Rights, the possession by a Party of the right to transfer or grant a license, sublicense or other rights to such Know-How or Patent Rights (before giving effect to the rights granted by one Party to the other Party pursuant to this Agreement), without violating the terms of any agreement or arrangement with any Third Party.

"**Court**" means any court or arbitration tribunal of the United States, any domestic state, or any foreign country, and any political subdivision thereof.

"**Development Plan**" means the plan setting forth the development activities to be undertaken by Buyer. The initial Development Plan as of the Closing Date is attached hereto as Schedule 1.1(i).

"**Distributor**" means any Third Party which purchases its requirements for a Product in a country from Buyer or its Affiliates or Licensees and is appointed as a distributor to distribute, market and resell such Product in such country, even if such Third Party is granted ancillary rights to develop, package or obtain Regulatory Approvals of such Product in order to distribute, market or sell such Product in such country.

"**Dollar**" means United States dollar, and "$" shall be interpreted accordingly.

"**EMA**" means the European Medicines Agency or any successor agency or authority thereto.

"**Encumbrance**" means any encumbrance, claim, mortgage, pledge, assessment, security interest, option, license, right of first refusal or preemptive right, hypothecation, equitable interest, preference, right of possession, deed of trust, lease, lien, levy, restriction on transferability, defect in title, charge or other encumbrance of any kind, whether voluntarily incurred or arising by operation of applicable Law, any obligation to pay Taxes, any conditional sale or title retention agreement or other agreement granting any of the foregoing in the future or otherwise.

"**Equity Agreement**" means the Preferred Stock Purchase Agreement entered into on the date hereof.

"**EU 5 Countries**" means United Kingdom, Germany, France, Spain and Italy.

"**Existing Inventory**" means certain existing inventory for a Program as set forth on Schedule 1.1(e).

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

"**FDCA**" means the United States Federal Food, Drug, and Cosmetic Act, as amended from time to time, including additions, supplements, extensions, and modifications thereto.

"**Field**" means any therapeutic, prophylactic, preventative or diagnostic use in or for animals, including humans.

"**First Commercial Sale**" means, with respect to any Product in any country in the Territory, the first invoiced commercial sale, transfer or disposition for monetary value for use or consumption of that Product in that country after Regulatory Approval for that Product has been received in that country; *provided*, *that*, the following shall not constitute a First Commercial Sale: (a) any sale to an Affiliate or licensee (unless the Affiliate or licensee is the last entity in the distribution chain of the Product) or (b) any transfers of a Product without consideration or for nominal consideration for use in any clinical trial, or for any bona fide charitable, compassionate use or indigent patient program purpose where Products are sold at or below cost of goods sold, or as a sample.

"**Force Majeure**" means any occurrence beyond the reasonable control of a Party, including any act of God, flood, fire, explosion, earthquake, strike, lockout, quarantine, epidemic, labor dispute, casualty or accident, or war, revolution, civil commotion, act of terrorism, blockage or embargo, or any injunction, law, order, proclamation, regulation, ordinance, demand or requirement of any Governmental Entity or of any subdivision, authority or representative of any such Governmental Entity.

"**FTE**" means the equivalent of a full-time individual's work time actually spent on the performance of activities under this Agreement over a twelve (12) month period (including normal vacations, sick days and holidays) based on [***] hours worked per twelve (12)-month period. In no event shall one person be counted as more than one FTE.

"**FTE Rate**" means a rate of [***] per FTE per year.

"**Fundamental Representations**" means the representations and warranties set forth in Sections [***].

"**Generic Product**" means, with respect to a particular Product and regulatory jurisdiction, any pharmaceutical product that is sold by a Third Party (other than a Licensee) in such regulatory jurisdiction and that (a) contains the same Program Molecule as such Product; and (b) has obtained marketing authorization for use pursuant to a Regulatory Approval process governing approval of generic or interchangeable drugs based on the then-current standards in such regulatory jurisdiction; and (c) has been deemed by the applicable Regulatory Authority as substitutable for such Product in such country.

"**Governmental Entity**" means any court, tribunal, arbitrator, Regulatory Authority, agency, commission, department, ministry, official or other instrumentality of the United States or other country, or any supra-national organization, or any foreign or domestic, state, county, city or other political subdivision.

"**IND**" means (a) an Investigational New Drug Application (as defined in the FDCA and the regulations promulgated thereunder) or any successor application or procedure required to initiate

clinical testing of a therapeutic product in humans in the United States; (b) the equivalent of an Investigational New Drug Application that is required in any other country or region before beginning clinical testing of a therapeutic product in humans in such country or region (including any Clinical Trial Authorization required to initiate clinical testing of a therapeutic product in humans in the United Kingdom); and (c) all supplements and amendments to any of the foregoing.

"**Indemnified Party**" means a Seller Indemnified Party or Buyer Indemnified Party, as the case may be.

"**In-Licensed Patent Rights**" means the Patent Rights licensed under an Assigned Agreement.

"**Know-How**" means, collectively, any knowledge, information, techniques, technology, trade secrets, inventions (whether patentable or not), discoveries, methods, know-how, data and results, including all technical, scientific, pre-clinical, clinical and regulatory data (including pharmacological, biological and toxicological data and results), analytical and quality control data and results and other information, but excludes Patent Rights with respect to any of the foregoing.

"**Knowledge**" means, with respect to Seller, the actual knowledge of a fact or other matter of [***] for the applicable Program.

"**Law**" means any federal, state, local or foreign law, statute, code or ordinance, treaties (including tax treaties) or any rule or regulation promulgated by any Governmental Entity including all decisions of any Courts having the effect of law in each such jurisdiction.

"**Liability**" means any and all debts, liabilities and obligations, whether known or unknown, asserted or unasserted, determinable or otherwise, accrued or fixed, absolute or contingent, liquidated or unliquidated, incurred or consequential, or matured or unmatured, including those arising under any Law, Litigation, Order, or Contract.

"**Licensee**" means any Third Party to which Buyer grants a license under the Assigned Intellectual Property, a sublicense under Patent Rights or Know-How licensed to Buyer under any of the Assigned Agreements, or a sublicense under any Patent Rights within the Licensed Intellectual Property, for the development, manufacture, use or commercialization of any Product, beyond the mere right to purchase any Product from or to provide services on behalf of Buyer or its Affiliates, but expressly excluding contract manufacturers and contract research or development organizations.

"**Litigation**" means any suit, action, arbitration, cause of action, claim, complaint, criminal prosecution, investigation, inquiry, demand letter, judicial, arbitration or other administrative proceeding, whether at law or at equity, before or by any Court, Governmental Entity, arbitrator or other tribunal.

"**Materials**" means the materials set forth on Schedule 1.1(c).

"**NDA**" means a New Drug Application, as defined in the FDCA, or any successor application or procedure required to sell any Product in the United States.

"**Net Sales**" means [***].

"**Order**" means any judgment, order, writ, injunction, ruling, stipulation, determination, award or decree of or by, or any settlement under the jurisdiction of, any Court or Governmental Entity.

"**Patent Assignment Agreement**" means the patent assignment agreement, substantially in the form attached as Exhibit C.

"**Patent Rights**" means the rights and interests in and to issued patents and pending patent applications (which, for purposes of this Agreement, include certificates of invention, applications for certificates of invention and priority rights) in any country or region, including any divisionals, continuations, continuations-in-part, substitutions, patents of addition, reissues, extensions, re-examinations or renewal applications related to, or claiming priority to, the foregoing (including any supplementary protection certificates) or any confirmation patent or registration patent, and all patents issuing on, and all foreign counterparts of, any of the foregoing.

"**Permitted Encumbrances**" means (a) statutory liens with respect to the payment of Taxes, in all cases which are not yet due or payable or that are being contested in good faith; (b) statutory liens of landlords, suppliers, mechanics, carriers, materialmen, warehousemen, service providers or workmen and other similar liens imposed by applicable Law created in the ordinary course of business the existence of which do not constitute a default or breach under any of the Assigned Agreements; (c) licenses under the Assigned Intellectual Property and In-Licensed Patent Rights granted as of the Closing Date under the Assigned Agreements, Delayed Assigned Contracts, Related Agreements, and Non-Assignable Contracts; and (d) licenses under later-discovered Assigned Intellectual Property subject to Section 2.11 under the Assigned Agreements, Related Agreements, and Non-Assignable Contracts; excluding any of the above liens (i) to the extent they relate to any activity prior to the Closing Date, or (ii) constituting Sellers Taxes.

"**Person**" means any natural person, corporation, general partnership, limited partnership, limited liability company, proprietorship, joint venture, other business organization, trust, entity, union, association or Governmental Entity.

"**Post-Closing Tax Period**" means any taxable period beginning after the Closing Date, and the portion of any Straddle Period beginning the day after the Closing Date.

"**Pre-Closing Tax Period**" means any taxable period (or portion of a Straddle Period) ending on or before the Closing Date.

"**Product**" means, as applicable, a TAK-228 Product or a TAK-659 Product.

"**Program**" means, as applicable, the Seller's program, as of the Closing Date, that is focused on developing (i) TAK-228 or (ii) TAK-659.

"**Program Molecule**" means, as applicable, TAK-228 or TAK-659.

"**Registrational Trial**" means a single randomized, placebo or active controlled human clinical trial of a Product on sufficient numbers of patients that is designed to demonstrate statistically that such Product is safe and efficacious for its intended use, to evaluate the risk-benefit relationship of such Product, and to define warnings, precautions and adverse reactions that are associated with such Product in the dosage range to be prescribed, as described in 21 C.F.R. §312.21(c) or corresponding foreign regulations, and that is intended to support obtaining Regulatory Approval of such Product, regardless of whether such trial is referred to as a "Phase 2 Trial", "Phase 2b Trial", "Phase 2[b]/3" or Phase 3 Trial. If a clinical trial of a Product is not initially designed as a Registrational Trial but is later re-designed, converted or expanded into such a trial (an "**Adjusted Registrational Trial**"), then it shall be deemed to be a Registrational Trial hereunder as of the date of such re-design, conversion or expansion. [***]

"**Regulatory Approval**" means the approval, license or authorization of the applicable Regulatory Authority necessary for the marketing and sale of a Product for a particular indication, and including the approval by the applicable Regulatory Authority of any expansion or modification of the label for such indication.

"**Regulatory Authority**" means any national, supra-national (e.g. the European Commission or the Council of the European Union), regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity with authority over the distribution, importation, exportation, manufacture, production, use, storage, transport, clinical testing, marketing, pricing or sale of a Product in such country or region in the Territory, including the FDA, the EMA, the Japanese Ministry of Health, Labour and Welfare and any successor entity thereto, the Pharmaceuticals and Medical Devices Agency of Japan and any successor entity thereto and the UK Medicines and Healthcare products Regulatory Agency in the United Kingdom and any successor entity thereto.

"**Regulatory Exclusivity**" means any exclusive marketing rights or data exclusivity rights conferred by any Governmental Entity with respect to a Product, other than Patent Rights, including rights conferred in the United States to a NDA holder under the Hatch-Waxman Act or the FDA Modernization Act of 1997 (including pediatric exclusivity), or rights similar thereto outside the United States.

"**Regulatory Filing**" means, collectively: (a) any IND, Marketing Authorization Application (MAA), drug master file, application for designation as an "Orphan Drug" under the Orphan Drug Act, for "Fast Track" status under Section 506 of the FDCA (21 U.S.C. § 356) or for a Special Protocol Assessment under Section 505(b)(4)(B) and (C) of the FDCA (21 U.S.C. § 355(b)(4)(B)) and all other similar filings (including counterparts of any of the foregoing in any country or region in the Territory); (b) all supplements and amendments to any of the foregoing; and (c) all data and other information contained in, and correspondence relating to, any of the foregoing.

"**Regulatory Materials**" means the materials set forth on Schedule 1.1(d). For clarity, Regulatory Materials relating to a Program Molecule in combination with a Takeda Compound are explicitly excluded.

"**Seller Taxes**" means (a) all Taxes of Seller or its Affiliates, or for which the Seller or any of its Affiliates is or are liable (including as a transferee or successor, or by contract or otherwise by operation of Law), for any taxable period (including any Tax of the Seller or any of its Affiliates that becomes a Liability of Buyer under any common law doctrine of de facto merger or transferee or successor liability or otherwise by operation of contract or Law), and (b) all Taxes relating to the ownership of the Acquired Assets for any Pre-Closing Tax Period, including the portion of any Straddle Period ending on the relevant Assignment Date as determined by Section 5.8.7.

"**Straddle Period**" means any taxable period that begins on or before but does not end on the relevant Assignment Date.

"**TAK-228**" means (a) the small molecule internally coded by Seller as TAK-228 (also referred to as sapanisertib, INK128 and MLN0128), which has the structure set forth on Schedule 1.1(a), (b) any compound that falls within the scope of the claims, or is otherwise disclosed, in an Assigned Patent Right that also claims or discloses the molecule described in the foregoing clause (a), or (c) any salt, free acid or base, complex, solvate, hydrate, isotope, polymorph, stereoisomer, tautomer, ester, polymorph, stereoisomer, metabolite or prodrug of (a) or (b).

"**TAK-659**" means (a) the small molecule internally coded by Seller as TAK-659 (also referred to as mivavotinib), which has the structure set forth on Schedule 1.1(b), (b) any compound that

falls within the scope of the claims, or is otherwise disclosed, in an Assigned Patent Right that also claims or discloses the molecule described in the foregoing clause (a), or (c) any salt, free acid or base, complex, solvate, hydrate, isotope, polymorph, stereoisomer, tautomer, ester, polymorph, stereoisomer, metabolite or prodrug of (a) or (b).

"**TAK-228 Product**" means any product that contains or comprises TAK-228, alone or in combination with one or more Additional Active(s), in any formulation or dosage form and for any mode of administration; *provided that*, in no event will any TAK-228 Product include any Takeda Compounds.

"**TAK-659 Product**" means any product that contains or comprises TAK-659, alone or in combination with one or more Additional Active(s), in any formulation or dosage form and for any mode of administration; *provided that*, in no event will any TAK-659 Product include any Takeda Compounds.

"**Takeda Compound**" means any compound or molecule owned or Controlled by Seller or its Affiliates (including any such compound or molecule that has been exclusively licensed by Seller or its Affiliates), but excluding any Program Molecule.

"**Tax**" or "**Taxes**" means any federal, state, local or foreign income, gross receipts, branch profits, license, payroll, employment, excise, severance, stamp, occupation, premium, windfall profits, escheat, environmental, customs duties, capital stock, franchise, profits, withholding, social security, unemployment, disability, real property, personal property, sales, use, transfer, registration, ad valorem, value added, alternative or add-on minimum or estimated tax or other tax of any kind whatsoever, including any interest, penalty or addition thereto, whether disputed or not and including any obligation to indemnify or otherwise assume or succeed to the tax liability of any other Person by Law, by Contract or otherwise.

"**Tax Return**" means any return, declaration, notice, statement, claim for refund, report or form (including any schedule or attachment thereto) or other document filed or required to be filed with respect to Taxes and including all amendments or supplements thereof.

"**Territory**" means worldwide.

"**Third Party**" means a Person other than Buyer, Seller or their respective Affiliates.

"**US GAAP**" means United States Generally Accepted Accounting Principles.

"**Valid Claim**" means (a) any claim of an issued and unexpired patent within the Assigned Patent Rights, [***] or In-Licensed Patent Rights that has not been held unpatentable, invalid or unenforceable by a decision of a Court or other Governmental Entity of competent jurisdiction, unappealable or unappealed within the time allowed for appeal, and which has not been cancelled, withdrawn, revoked, abandoned or admitted to be invalid or unenforceable through reissue, disclaimer or otherwise, or (b) a claim of a pending patent application included within the Assigned Patent Rights, [***] or In-Licensed Patent Rights that is being prosecuted in good faith and has not lapsed, been abandoned, been cancelled or revoked, or been deemed unenforceable or invalid by a non-appealable decision or an appealable decision from which no appeal was taken within the time allowed for such appeal of a Court or other Governmental Entity of competent jurisdiction, which claim has not been pending for more than [***] years from [***].

1.2 **Additional Definitions**. In addition, each of the following definitions shall have the respective meanings set forth in the section of this Agreement indicated below:

Definition	Section

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1.3 **Construction of Certain Terms and Phrases**. Unless the context of this Agreement otherwise requires: (a) words of any gender include each other gender; (b) words using the singular or plural number also include the plural or singular number, respectively; (c) the terms "hereof," "herein," "hereby" and derivative or similar words refer to this entire Agreement; (d) the terms "Article" or "Section" refer to the specified Article or Section of this Agreement; (e) the term "or" has, except where otherwise indicated, the inclusive meaning represented by the phrase "and/or"; (f) the term "including" means "including without limitation"; and (g) whenever this Agreement refers to a number of days, such number shall refer to calendar days unless Business Days are specified.

ARTICLE 2.
PURCHASE AND SALE OF ASSETS

2.1 **Closing**. The consummation (the "**Closing**") of the transactions contemplated by this Agreement and the Ancillary Agreements will take place remotely via the exchange of documents and signatures (or at such other time and place as the Parties mutually agreed upon, orally or in writing), as promptly as practicable following the execution of this Agreement, assuming the satisfaction or waiver (by the Party entitled to the benefit of such condition) of the conditions set forth in Section 2.2 (other than conditions that by their nature are to be satisfied at the Closing, but subject to the satisfaction or waiver of such conditions). The date on which the Closing occurs is referred to herein as the "**Closing Date**".

2.2 **Closing Deliveries**.

2.2.1 On or prior to the Closing Date, Seller shall deliver to Buyer the following:

(a) the Bill of Sale, duly executed by Seller;

(b) the Equity Agreement, duly executed by Seller;

(c) the Patent Assignment Agreement, duly executed by Seller; and

(d) such other documents and instruments of transfer as Buyer and Seller mutually agree are necessary to evidence or effectuate the transactions contemplated by this Agreement and the Ancillary Agreements.

2.2.2 On or prior to the Closing Date, Buyer shall deliver to Seller the following:

(a) the Bill of Sale, duly executed by Buyer;

(b) the Patent Assignment Agreement, duly executed by Buyer;

(c) the Equity Agreement, duly executed by Buyer; and

(d) such other documents and instruments of transfer as Buyer and Seller mutually agree are necessary to evidence or effectuate the transactions contemplated by this Agreement and the Ancillary Agreements.

2.3 **Purchase and Sale of Assets**. Subject to the terms and conditions set forth in this Agreement, Seller hereby sells, conveys, assigns, transfers and delivers to, and shall cause its Affiliates to

sell, convey, assign, transfer and deliver to, Buyer, and Buyer hereby purchases and acquires from each of Seller or its Affiliates, as the case may be, all of Seller's and its Affiliates' right, title and interest in and to the assets described or set forth on Schedule 2.3 attached hereto (collectively, the "**Acquired Assets**"), free and clear of all Encumbrances (other than Permitted Encumbrances).

2.4 **Excluded Assets**. No right, title or interest is being sold, assigned, transferred, conveyed or delivered to Buyer in or to (a) any of the property and assets of Seller other than the Acquired Assets, or (b) any rights or claims of Seller under this Agreement (collectively, the "**Excluded Assets**"). For the avoidance of doubt, Excluded Assets include the assets set forth in Schedule 2.4.

2.5 **License Back**. Buyer hereby grants Seller and its Affiliates (a) a non-exclusive, non-transferable, royalty-free, fully paid-up license under the Assigned Intellectual Property, with the right to sublicense solely to those counterparties to the Related Agreements and Non-Assignable Contracts to whom Seller had granted a license under the Assigned Intellectual Property prior to the Closing Date, solely as necessary for Seller or its Affiliate to perform Seller's obligations under this Agreement and any Ancillary Agreement (including the continued performance of any Related Agreement or Non-Assignable Contract), and (b) a non-exclusive, irrevocable royalty-free, fully paid-up license, with the right to sublicense to service providers and the like conducting activities on behalf of Seller or its Affiliate, under the Assigned Intellectual Property for [***] research purposes. Each sublicense shall be consistent with the terms and conditions of this Agreement, including requiring each such sublicensee to assign or license Transaction IP to Seller and to protect and keep confidential any Confidential Information of the Parties in accordance with Article 7 of this Agreement. For clarity, the license in the foregoing clause (a) includes the right to manufacture until [***], Product that is necessary to perform Seller's supply obligations existing as of the Closing Date under Related Agreements and Non-Assignable Contracts. If Seller requires a sublicense under any intellectual property licensed under an Assigned Agreement to perform its obligations under this Agreement or any Ancillary Agreement, the Parties will enter into a separate sublicense agreement. Any Know-How or Patent Rights that arise from the practice of the license granted pursuant to clause (b) above shall be referred to as "**Section 2.5(b) IP**".

2.6 **Licensed Intellectual Property**. To the extent Seller or its Affiliate Controls any Patent Rights or Know-How (a) as of the Closing Date; or (b) on or after the Closing Date and (A) included in the Transaction IP, (B) Controlled pursuant to a Non-Assignable Contract or Related Agreement, in each case (A) and (B) pursuant to Section 4.3, or (C) constituting Section 2.5(b) IP, that in each case (a) and (b) are necessary to research and develop, make, have made, use, sell, offer for sale, and import Products (including researching, developing, and making Program Molecules for the purpose of exercising such license with respect to Products) in the Field in the Territory and that are not included in Assigned Intellectual Property or licensed under the Assigned Agreements ("**Licensed Intellectual Property**"), Seller hereby grants Buyer a non-exclusive license under and to such Licensed Intellectual Property, with the right to grant sublicenses through multiple tiers, for the sole purpose of researching, developing, making, have made, using and importing Program Molecules and researching and developing, making, having made, using, selling, offering for sale, and importing Products in the Field in the Territory; provided, that Licensed Intellectual Property does not include any Patent Rights or Know-How that [***]. Each sublicense shall be consistent with the terms and conditions of this Agreement, including requiring each such sublicensee to protect and keep confidential any Confidential Information of the Parties in accordance with Article 7 of this Agreement. For clarity, Licensed Intellectual Property, other than Section 2.5(b) IP, does not include Patent Rights or Know-How owned by Seller or its Affiliate that solely relate to either Program Molecule, which is included in Assigned Intellectual Property. Schedule 2.6 sets forth the Licensed Intellectual Property as of the Closing Date; such schedule may be updated by the Parties from time to time. Without limiting the foregoing, with respect to Patent Rights included in Section 2.5(b) IP, Buyer shall have the right to notify Seller that it desires to obtain an exclusive license with respect thereto for the sole purpose of researching, developing, making, have made, using and importing Program Molecules and researching

and developing, making, having made, using, selling, offering for sale, and importing Products in the Field in the Territory, and upon receipt of any such notification the Parties shall negotiate [***] an exclusive license to the extent that Seller has the right and ability to grant such a license; provided that neither Party has an obligation to enter into any such exclusive license.

2.7 **Post-Closing Liabilities**. Subject to the terms and conditions of this Agreement, including Section 3.5.3, on the Closing Date, Buyer shall assume and, in any event, otherwise agrees to pay, perform and discharge all Liabilities arising (a) under the Assigned Agreements on or after the applicable Assignment Date as a result of activities performed under any such Assigned Agreements on or after the applicable Assignment Date, (b) or resulting from the research, development, making, having made, using, and importing or other exploitation of the Products or other Acquired Assets by or on behalf of Buyer, to the extent that such Liability arises from any event, condition or circumstance occurring on or after the Closing Date, and (c) or resulting from Buyer's breach of Section 3.6 with respect to Related Agreements, except in each case (a), (b) and (c) to the extent such Liabilities arise or result from the Seller's or its Affiliate's or its or their (sub)licensee's (other than Buyer's or its Affiliate's or its or their (sub)licensee's) act or omission (the "**Post-Closing Liabilities**").

2.8 **Excluded Liabilities**. Subject to the terms and conditions of this Agreement, including Section 3.5.3, on the Closing Date Seller shall retain, and shall be responsible for paying, performing and discharging when due, and Buyer shall not assume or have any responsibility for paying, performing or discharging, any Liabilities of Seller and its Affiliates other than the Post-Closing Liabilities to the extent that such Liabilities do not arise or result from the Seller's or its Affiliate's or its Affiliate's or its or their (sub)licensee's acts or omissions (the "**Excluded Liabilities**"). Without limiting the foregoing, neither Buyer nor its Affiliates shall be obligated to assume, and none of them do assume, and each of them hereby disclaims responsibility for, any of the following Liabilities of Seller and its Affiliates to the extent that such Liabilities do not arise or result from the Buyer's or its Affiliate's or its or their (sub)licensee's (other than Seller's or its Affiliate's or its or their (sub)licensee's) acts or omissions:

2.8.1 any Liabilities of Seller or any of its Affiliates attributable to any asset, property or right that is not included in the Acquired Assets or Licensed Intellectual Property;

2.8.2 any Liabilities of Seller or any of its Affiliates attributable to the research, development, making, having made, using, and importing or other activity by Seller or any Affiliate related to the Acquired Assets on or prior to the Closing Date (except for Assigned Agreements, which will be on or prior to the applicable Assignment Date), including any obligations to pay for goods and services [***] in the ordinary course of either of the Programs as a result of [***] prior to the Closing Date (or the applicable Assignment Date);

2.8.3 any Liabilities of Seller or any of its Affiliates attributable to its use or exercise of the licenses set forth in Section 2.5;

2.8.4 all Liabilities of Seller or any of its Affiliates for Seller Taxes;

2.8.5 all Liabilities of Seller or any of its Affiliates [***] under the Related Agreements; and

2.8.6 all Liabilities of Seller or any of its Affiliates [***] under the Assigned Agreements as a result of [***] prior to the applicable Assignment Date or as a result of [***] prior to the applicable Assignment Date to the extent that such Liabilities are not attributable to any failure by Buyer or any of its Affiliates to comply with the terms thereof on or after the applicable Assignment Date.

2.9 **Adverse Events**. From and after the transfer of the IND and the global safety database for each Product, which will occur [***] after the Closing, Buyer will assume all responsibility for reporting adverse events involving such Product arising on or after such transfer or otherwise known to Buyer to the applicable Governmental Entity as promptly as practicable and in any event in the timeframe required by Law. Following the Closing Date and upon one Party's notice to the other, in accordance with a timeline to be agreed by the Parties, the Parties shall enter into a pharmacovigilance / safety data exchange agreement to facilitate the exchange of safety data from studies relating to a Program Molecule to the extent necessary to permit each Party to satisfy applicable reporting obligations; provided, that, safety data [***]; provided, further, however, that if Buyer (or its Affiliate or its or their (sub)licensee) is required by a Regulatory Authority to report any safety data relating solely to a Program Molecule that [***], Seller will cooperate with Buyer to make such information available to such Regulatory Authority. For further clarity, it is anticipated that any such agreement will only be required for so long as any applicable data or information is required or generated in connection with any Related Agreement or Non-Assignable Contract. In the event Buyer (or its Affiliate or Licensee) is required by a Regulatory Authority to report any safety data relating to a Program Molecule that was the subject of a combination study, the pharmacovigilance / safety data exchange agreement will provide for Seller to cooperate with Buyer to make such information available to Buyer and to such Regulatory Authority.

2.10 **Transition Assistance**. During the period from the Closing Date until the latest of (a) [***], Seller shall reasonably cooperate with Buyer to facilitate an orderly transition of the Programs to Buyer, including providing reasonable amounts of consultation regarding the Assigned Assets and the status of the Programs, and Buyer shall cooperate with Seller to facilitate the receipt of such transition. Seller's assistance obligation pursuant to this Section 2.10 is limited to [***]. Buyer shall reimburse Seller for both reasonable and documented, to the extent a given cost exceeds [***], out-of-pocket costs and internal costs (calculated by reference to the number of hours of support provided at the hourly FTE Rate) incurred by Seller or its Affiliates to provide such transition assistance, except for the internal cost for the first [***] of support and assistance from Seller or its Affiliates, which shall be provided at Seller's cost. Buyer shall pay or reimburse, as applicable, such costs and charges as such may be invoiced by Seller to Buyer from time-to-time within [***] days of receipt of such an invoice. Seller's assistance under this Section 2.10 shall include payment of any fees for maintaining the Assigned Patent Rights that are due within [***] after the Closing Date, which fees will be passed through to, and reimbursed by, Buyer.

2.11 **Later-Discovered Assigned Intellectual Property, Assigned Agreements and Licensed Intellectual Property**. If at any time after the Closing Date, either Party becomes aware of any Assigned Intellectual Property or Licensed Intellectual Property that was not included on the schedules hereto or was not transferred to Buyer, or any Contract to which Seller or its Affiliate is a Party that relates solely to either or both Programs and is not included in the Assigned Agreements (and is not otherwise expressly identified as a Related Agreement), such Party shall notify the other Party, and Seller shall promptly thereafter take actions reasonably necessary to transfer such Assigned Intellectual Property to Buyer, to assign such Contract to Buyer and with respect to Licensed Intellectual Property, to enable Buyer to exploit its rights thereto pursuant to this Agreement. Any such assigned Contract will be deemed an Assigned Agreement. If at any time after the Closing Date, either Party becomes aware of any asset that was transferred to Buyer as an Acquired Asset but is ultimately determined to be an Excluded Asset, or Buyer is found to be in possession of any Excluded Asset, such Party shall notify the other Party, and Buyer shall promptly thereafter take actions reasonably necessary to transfer such Excluded Asset(s) to Seller.

2.12 **Approval [***]**. Prior to the [***] anniversary of the Closing Date, Buyer shall not [***], without Seller's prior written approval [***]. From and after the [***] anniversary of the Closing Date, Seller will no longer have such approval right.

ARTICLE 3.
DEVELOPMENT AND COMMERCIALIZATION OF PRODUCTS; ONGOING OBLIGATIONS

3.1 **Responsibility**. Buyer shall have the sole right and responsibility, at its sole cost and expense, for the conduct, itself or with or through any Affiliate or Licensee, of all research, development, regulatory, manufacturing and commercialization activities applicable to the Program Molecules or any Product for use in the Field and in the Territory after the Closing Date.

3.2 **Diligence**. Buyer shall [***] research and develop, including to obtain Regulatory Approval for, and upon obtaining Regulatory Approval to commercialize at least one (1) TAK-228 Product and at least one (1) TAK-659 Product in each of [***]. Buyer shall (a) perform its obligations in good scientific manner and in compliance with all applicable Law in all material respects and (b) notify Seller in writing if it and its Affiliates and Licensees (i) have determined to permanently discontinue, or (ii) plan to [***], all research, development and/or commercialization activities and efforts with respect to all TAK-228 Products or all TAK-659 Products. Seller may deliver Buyer a written notice if it believes Buyer has breached its obligation under this Section 3.2, setting forth the basis for such belief, and Buyer shall respond to such notice with a written description of the activities it is conducting with respect to its obligations under this Section 3.2 within [***] of receipt of such notice.

3.3 **Reports**.

3.3.1 **Records; Reports**. Buyer shall (a) maintain records of its research, development, manufacture and commercialization activities with respect to the Program Molecules and Products under this Agreement in sufficient detail and in good scientific manner, which shall reflect work performed and results achieved in the conduct of such research, development, manufacture and commercialization activities, and (b) keep Seller reasonably informed regarding the research, development and manufacturing activities conducted with respect to Program Molecules and Products by providing Seller with [***] reports until [***] of one (1) TAK-228 Product (with respect to activities regarding TAK-228 Product) and one (1) TAK-659 Product (with respect to activities regarding TAK-659 Product) summarizing the activities undertaken by Buyer, its Affiliates and its Licensees since the last report and providing the then-current [***] to be undertaken (each, a "**Report**"); provided that, at Seller's sole discretion, Seller may provide written notice to Buyer prior to the due date of the Report(s) that it does not wish to receive such Report(s) and Buyer shall cease providing Reports until such time, if ever, that Seller provides written notice Buyer that it desires to start receiving the Reports again, at which time Buyer shall again begin providing Reports in accordance with this Section 3.3.1.

3.3.2 **Content of Reports**. Each Report provided pursuant to Section 3.3.1 will include at least information regarding: [***]. In addition, on a Product-by-Product basis, on an annual basis commencing on or about January 31 of the first Calendar Year following the first Calendar Year during which [***]. All information and documents provided by Buyer under this Section 3.3.2 will be Confidential Information of Buyer.

3.3.3 At least [***] days prior to initiating (or publicly announcing, if earlier) any clinical trial of a Product sponsored by Buyer, its Affiliate or its Licensee, or sponsored by a Third Party and for which Buyer, its Affiliate or its Licensee supplies Program Molecule, that involves one (1) or more of Seller's or its Affiliate's products (marketed or otherwise), Buyer shall report to Seller in writing of such intention and name the relevant product(s) and the Product(s) it intends to use in such clinical trial.

3.4 **Audit.** Buyer will keep complete and accurate records of Buyer and its Affiliates in reasonably sufficient detail to permit Seller to confirm the accuracy of the calculation of earn-out payments under Section 5.2 and Sales Milestone Payments under Section 5.4 for [***] years after the Calendar Year

to which such records pertain. At the request of Seller, Buyer shall permit an independent auditor designated by Seller and reasonably acceptable to Buyer, at reasonable times and upon reasonable notice, to audit the books and records maintained pursuant to the preceding sentence to ensure the accuracy of all financial reports and payments made hereunder. Such examinations may not be conducted more than once in any [***] period (unless a previous audit during such [***] period revealed a failure to pay Sales Milestone Payments or an underpayment of more than [***] from the reported amounts with respect to such period) and may not include records previously audited under this Section 3.4 (unless such previously audited records revealed a failure to pay Sales Milestone Payments or an underpayment of more than [***] from the reported amounts with respect to such period). Such auditor shall enter into a confidentiality agreement with Buyer and shall not disclose Buyer's confidential information, except (a) to disclose the findings and results of the audit to Seller and (b) to the extent such disclosure is necessary to verify the accuracy of the financial reports furnished by Buyer or the amounts of such payments due by Buyer under this Agreement. Except as provided below, the cost of this audit shall be borne by Seller, unless the audit reveals an under-reporting by Buyer of more than [***] from the amounts due for the audited period, in which case Buyer shall bear the cost of the audit.

3.5 **Assumption of Rights and Obligations under Assigned Agreements**.

3.5.1 Buyer acknowledges that certain intellectual property is in-licensed under the Assigned Agreements and that the practice of such in-licensed intellectual property will be subject to the terms and conditions of the applicable Assigned Agreement.

3.5.2 Buyer acknowledges and agrees that [***].

3.5.3 [***]

3.6 **Related Agreements**. Agreements to which Seller or its Affiliate is a party that relate to a Program Molecule but that are not included in the Assigned Agreements are referred to herein as "Related Agreements" and are, to the extent Known by Seller to have been identified by Seller as of the Closing Date, set forth in Schedule 3.6. Seller shall provide to Buyer, promptly after receipt thereof, all data related to any Program Molecule that is generated under the Related Agreements and that Seller receives from a given counterparty to any such Related Agreement, which data will be included in the Assigned Know-How or Licensed Intellectual Property, as applicable; provided, that except as follows, Seller shall not be obligated to provide any data involving a [***]. Upon Buyer's request, Seller will provide to Buyer copies of any data Controlled by Seller that is related to a Program Molecule [***]. `In addition, Seller shall use commercially reasonable efforts to maintain the Related Agreements in full force and effect in accordance with their terms and conditions and without any further amendment that would adversely affect the rights of Buyer as contemplated herein, except with Buyer's prior written consent. Buyer shall assist Seller in Seller's performance of the Related Agreements, as and to the extent reasonably requested by Seller, including supplying Product; provided, that if Seller requests Buyer's assistance in excess of [***], then Seller shall reimburse Buyer for internal costs (calculated by reference to the number of hours of support provided at the hourly FTE Rate) incurred by Buyer or its Affiliates to provide such excess assistance. Seller shall pay such costs as such may be invoiced by Buyer to Seller from time-to-time within [***] of receipt of such an invoice. If Buyer reasonably requests that Seller supply Product for purposes of performing Seller's obligations under the Related Agreement, then the Parties shall promptly negotiate appropriate terms and conditions to govern such supply (including providing such Product at no charge).

3.7 **Non-Assignable Contract**.

3.7.1 If any Contract that solely relates to either or both Programs (other than Related Agreements) is not assignable or transferable (each, a "**Non-Assignable Contract**") without the consent of, or waiver by, a Third Party or action by a Governmental Entity (each, an "**Assignment Consent**"), either as a result of the provisions thereof or applicable Laws, and any such Assignment Consent is not obtained on or prior to the Closing Date, then this Agreement and the related instruments of transfer shall not constitute an assignment or transfer of such Non-Assignable Contract and such Non-Assignable Contract shall not be included in the Acquired Assets unless and until such Assignment Consent is obtained. Each of the Parties hereto, for a period of [***] following the Closing Date, or in the case of the [***] (as defined in Schedule 3.9), until the Assignment Consent is obtained (the "**Cooperation Period**"), shall use commercially reasonable efforts to obtain all Assignment Consents for each Non-Assignable Contract; provided, however, that nothing in this Section 3.7.1 shall require Seller or any of its Affiliates to modify any of its respective rights in a manner adverse to Seller or any of its Affiliates or to pay any fee or other payment, or incur any Liability, to the counterparty of any Non-Assignable Contract in connection with the efforts set forth in this Section 3.7.1 and, for clarity, to the extent any such payment would be required and Buyer refuses to provide such payment, then it would be commercially reasonable for Seller to cease further efforts. To the extent such Assignment Consents are obtained during the Cooperation Period, Seller hereby sells, conveys, assigns, transfers and delivers to, and shall cause its Affiliates to sell, convey, assign, transfer and deliver to, Buyer, and Buyer hereby purchases and acquires from each of Seller or its Affiliates, such Non-Assignable Contract. Following any such assignment, such assets shall be deemed Assigned Agreements and Acquired Assets for purposes of this Agreement.

3.7.2 Until the expiration of the Cooperation Period, Seller shall cooperate with Buyer [***] to provide Buyer or its designee with the net benefits of each Non-Assignable Contract after the Closing as if the appropriate Assignment Consents had been obtained, including by granting rights and establishing arrangements whereby Buyer shall undertake the work necessary to perform under such Non-Assignable Contract. To the extent the benefits of a Non-Assignable Contract are made available to Buyer during the Cooperation Period, Buyer shall perform, at the reasonable direction of Seller, the obligations of Seller under such Non-Assignable Contract and assume all Liabilities arising under such Non-Assignable Contract on or after the Closing Date to the extent that such Liabilities are not attributable to the failure by Seller or any of its Affiliates to comply with the terms thereof prior to the Closing, and economically bear any out-of-pocket additional costs in connection with Buyer's or its Affiliate's performance under such Non-Assignable Contract. Buyer will provide to Seller all safety data related to a Program Molecule and generated by or on behalf of Buyer and necessary for Seller to comply with its obligations under any Non-Assignable Contract.

3.8 **Cooperation in Combination Clinical Study(ies)**. Upon Seller's request, the Parties shall negotiate in good faith the terms under which the Parties would conduct one (1) or more combination clinical study(ies) involving a Product and one (1) or more products of Seller, such terms to include, unless otherwise agreed by the Parties, rights of access to, ownership of and terms related to data ownership and use (which will not be subject to the terms of this Agreement), having Seller be the sponsor of such combination clinical study(ies), terms for the supply of Product by Buyer and applicable products of Seller and grant of the appropriate licenses in order to conduct such study(ies). Buyer shall not be obligated to [***].

3.9 **Delayed Assignment of Contracts for Clinical Studies**. The Parties agree that any Contract listed on Schedule 3.9 (a "**Delayed Assigned Contract**") will not be assigned to Buyer, and will not be considered an Assigned Agreement, until the date on which the IND for such Program Molecule is transferred to Buyer (the "**Assignment Date**" for such Assigned Agreement). Seller hereby sells, conveys, assigns, transfers and delivers to, and shall cause its Affiliates to sell, convey, assign, transfer and deliver to, Buyer, and Buyer hereby purchases and acquires from each of Seller or its Affiliates, as of the applicable Assignment Date, each Delayed Assigned Contract. From and after the Assignment Date for any Delayed

Assigned Contract, such Delayed Assigned Contract shall be deemed an Assigned Agreement. For any Assigned Agreement that is assigned on the Closing Date, the Assignment Date for such Assigned Agreement will be the Closing Date. Seller shall use commercially reasonable efforts to comply with all terms and conditions of, and shall use commercially reasonable efforts to maintain in full force and effect, each Delayed Assigned Contract until the Assignment Date thereof, and shall not terminate or amend any Delayed Assigned Agreement without Buyer's prior written consent. Seller shall notify Buyer promptly upon becoming aware of any party's breach of any Delayed Assigned Contract, shall provide a copy of any notices delivered or received thereunder, and shall use commercially reasonable efforts to enforce any Delayed Assigned Contract against the counterparty.

ARTICLE 4.
CONTROL OF ASSIGNED PATENT RIGHTS

4.1 **Control of Assigned Patent Rights**.

4.1.1 From and after the Closing, Buyer, acting through patent counsel or agents of its choice, shall be solely responsible, in its sole discretion, for the preparation, filing, prosecution, maintenance, defense and enforcement of all Assigned Patent Rights throughout the Territory. All patent costs and expenses incurred by Buyer in connection with the preparation, filing, prosecution, maintenance, defense and/or enforcement of such Assigned Patent Rights shall be the sole responsibility of Buyer.

4.1.2 Buyer shall provide Seller at least once per Calendar Year an updated Schedule 1.1(h) – Part 1 and Schedule 1.1(h) – Part 2 showing the status of all Assigned Patent Rights and In-Licensed Patent Rights, respectively.

4.1.3 If Buyer decides to [***]

4.2 **Control of Licensed Intellectual Property**. Buyer will have no review, comment or step-in rights with respect to preparation, filing, prosecution, maintenance, defense or enforcement of any Licensed Intellectual Property. Seller shall be solely responsible, in its sole discretion, for such activities with respect to any Licensed Intellectual Property. If Seller discontinues the prosecution or maintenance of a patent application or patent within the Licensed Intellectual Property in any country or jurisdiction, then Seller shall provide Buyer with notice of such decision via a once per Calendar Year update (as and to the extent such update is needed to provide notice of any such discontinuance).

4.3 **Ownership of Transaction IP**. Ownership of any discovery or invention and intellectual property rights with respect thereto, developed through, or obtained in connection with, the performance of this Agreement or any Ancillary Agreements, but excluding any such discovery, invention and intellectual property rights that arise from the practice of the license granted pursuant to clause (b) of Section 2.5 ("Transaction IP") will be allocated based on inventorship in accordance with United States patent law. Seller's or its Affiliate's interest in any Transaction IP, and Seller's or its Affiliate's interest in any Know-How or Patent Rights it Controls pursuant to a Non-Assignable Contract or Related Agreement, shall be deemed to be either (a) Assigned Intellectual Property, to the extent owned by Seller or its Affiliate and solely relating to either or both Program Molecules (and thus assigned to Buyer pursuant to this Agreement), or (b) Licensed Intellectual Property, to the extent not solely relating to either or both Program Molecules (and thus licensed to Buyer pursuant to Section 2.6 of this Agreement) or in-licensed by Seller or its Affiliate.

ARTICLE 5.
PURCHASE PRICE AND OTHER PAYMENTS

5.1 **Upfront Consideration**. In partial consideration for the rights granted herein, including rights to the Acquired Assets, Buyer shall (a) pay Seller on the Closing Date an amount in cash equal to Ten Million Dollars ($10,000,000) by wire transfer of immediately available funds to the account(s) designated by Seller, and (b) issue One Million (1,000,000) shares of Buyer's Series A Preferred Stock, the number of shares to be valued at Thirty Five Million Dollars ($35,000,000), which issuance shall be subject to the terms and conditions set forth in the Equity Agreement.

5.2 **Payment of Earn-out Payments; Earn-Out Rates**.

5.2.1 **Earn-out Payment**. From and after the Closing, Buyer shall pay Seller an earn-out payment on the Annual Net Sales of all TAK-228 Products and an earn-out payment on the Annual Net Sales of all TAK-659 Products by or on behalf of Buyer, its Affiliates, or Licensees in a given Calendar Year (or partial Calendar Year), on a Product-by-Product basis, commencing with the First Commercial Sale of such Product in any country in the Territory, at the following rates:

Annual Net Sales Increment	**Earn-Out Payment Rate (%)**
For the portion of the Annual Net Sales of such Product in any given Calendar Year which is less than or equal to [***]	[***]
For the portion of the Annual Net Sales of such Product in any given Calendar Year which is greater than [***] but less than or equal to [***]	[***]
For the portion of the Annual Net Sales of such Product in any given Calendar Year which is greater than [***] but less than or equal to [***]	[***]
For the portion of the Annual Net Sales of such Product in any given Calendar Year which is greater than [***] but less than or equal to [***]	[***]
For the portion of the Annual Net Sales of such Product in any given Calendar Year which is greater than [***]	[***]

For purposes of clarity, (a) each earn-out payment rate will only apply to the corresponding tier of Annual Net Sales, and (b) the determination of the earn-out payment rate under this Section 5.2.1 shall be based on aggregate, worldwide Annual Net Sales of the relevant TAK-228 Products or the relevant TAK-659 Products in each Calendar Year.

5.2.2 **Expiration of Earn-Out Payments**. Such earn-out payments shall be payable on a Product-by-Product and country-by-country basis commencing upon the First Commercial Sale of such Product in such country in the Territory and continuing until the latest of (a) the expiration of the last-to-expire Valid Claim of the Assigned Patent Rights, the [***] and the In-Licensed Patent Rights covering or claiming such Product in such country, (b) expiration of Regulatory Exclusivity for such Product in such country, and (c) [***] years after First Commercial Sale of such Product in such country. Upon the expiration of the earn-out payment term with respect to a Product and a country, the license to Buyer under the Licensed Intellectual Property for such Product and in such country shall become fully-paid, perpetual and irrevocable.

5.2.3 **Earn-Out Payment Reduction**.

(a) On a Product-by-Product and country-by-country basis, if a Product is sold in a country in a Calendar Quarter when one (1) or more Generic Products for such Product are being sold in such country and such Generic Products account for at least [***] of the total [***] of both such Generic Products and such Product in such country for such Calendar Quarter, then, subject to Section 5.2.3(c) below, the earn-out payment applicable to the Net Sales of such Product sold in such Calendar Quarter shall be reduced by [***]. The determination of the units of the Generic Product(s) sold shall be based upon data provided by IQVIA (formerly IMS Health) or another mutually acceptable and reputable provider.

(b) Buyer shall bear all costs associated with securing licenses (that are in addition to any licenses under an Assigned Agreement) to any Third Party Patent Rights necessary to research and develop, make, have made, use, sell, offer for sale, or use any Product in the Territory. If it is necessary for Buyer to obtain or maintain a license from a Third Party to any Patent Rights owned by such Third Party (that are in addition to any licenses under an Assigned Agreement) in order to avoid infringement of such Patent Right [***] in the research and development, making, having made, using, selling, offering for sale, or importing or other exploitation of any Program Molecule or Product (excluding the part of a Combination Product that is not a Program Molecule or Product) in a country in the Territory and Buyer obtains or maintains such a license, then, subject to Section 5.2.3(c) below, Buyer shall have the right to deduct, from the earn-out payment that would otherwise have been due pursuant to Section 5.2.1 with respect to Net Sales of such Product in such country in a particular Calendar Quarter, an amount equal to [***] of the royalties paid by or on behalf of Buyer to such Third Party pursuant to such license on account of the sale of the Product in such country during such Calendar Quarter[***]. Notwithstanding the foregoing, for any Calendar Quarter in which the reduction under Section 5.2.3(a) applies, the reduction under this Section 5.2.3(b) for Third Party royalties paid during such Calendar Quarter may not be taken (on account of the floor under Section 5.2.3(c)) and may not be carried forward to subsequent Calendar Quarters. For clarity, payments under any Assigned Agreement are not deductible under this Section 5.2.3(b).

(c) Notwithstanding the foregoing Sections 5.2.3(a) and 5.2.3(b), in no event shall the aggregate earn-out payments payable under this Section 5.2 in a given Calendar Quarter with respect to a Product be reduced pursuant to Sections 5.2.3(a) and 5.2.3(b) by more than [***] cumulatively from the amounts that would otherwise be due if no such reductions applied.

5.2.4 **Earn-Out Payments and Reporting**. Buyer shall calculate all amounts payable to Seller pursuant to Section 5.2 at the end of each Calendar Quarter. Buyer will deliver to Seller (a) [***]; and (b) within [***] after the end of each Calendar Quarter, a written report setting forth the actual Net Sales for such Calendar Quarter and including the following information for such Calendar Quarter: (i) [***] (each, an "**Earn-Out Report**"). Upon receipt of such Earn-Out Report, Seller will issue an invoice to Buyer for the amount of the earn-out payments payable under this Section 5.2 set forth in such Earn-Out Report, which invoice will specify the amount of the earn-out payments payable under this Section 5.2 that should be made to Seller. Buyer will pay all earn-out payments payable under this Section 5.2 for a Calendar Quarter set forth in any such invoice within [***] after receipt of such invoice.

5.3 **Development Milestone Payments**. From and after the Closing, following the first achievement of each development milestone event set forth in the table below (each such event, a "**Development Milestone Event**"), Buyer shall pay, or cause to be paid, to Seller a one-time, non-refundable and non-creditable corresponding milestone payment (each, a "**Development Milestone Payment**") within [***] after receipt of invoice from Seller issued or on after the first achievement of such Development Milestone Event. Buyer shall notify Seller within [***] after each Development Milestone

Event is first achieved. For the avoidance of doubt, each Development Milestone Payment shall be payable one (1) time only for all TAK-228 Products and one (1) time only for all TAK-659 Products upon the first achievement of the corresponding Development Milestone Event, regardless of the number of times such Development Milestone Event may be achieved by the same or different Products. Notwithstanding anything to the contrary herein, multiple Development Milestone Events will not be deemed achieved for multiple Indications for TAK-659 Product as a result of the performance of the [***]. As used in the table below, "Indication" means an individual, separate and distinct disease or medical condition for which (a) at least one clinical trial is required to support inclusion of such disease or condition in the indication statement of a package insert approved by a Regulatory Authority for a Product or (b) a separate Marketing Authorization Application (or amendment or supplement thereto) must be filed. Indications of the same cancer type shall be deemed the same Indication unless they (i) have different organs of origin (e.g., gastric cancer and renal cancer would be different Indications), or (ii) are for a different hematological malignancy as classified by IDC10 codes (e.g., acute lymphoblastic leukemia, chronic myelogenous leukemia, non-Hodgkin's lymphoma, multiple myeloma, Hodgkin's disease, chronic lymphocytic leukemia and acute myeloid leukemia are all different Indications); provided that [***].

<table>
<tr><th colspan="6"><u>Development Milestone Payments</u></th></tr>
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*If a clinical trial [***].

5.4 **Sales Milestone Payments**. From and after the Closing, following the first achievement of each sales milestone event set forth in the applicable table below with respect to aggregate Annual Net Sales of all TAK-228 Products and aggregate Annual Net Sales of all TAK-659 Products (each such event, a "**Sales Milestone Event**"), Buyer shall pay, or cause to be paid, to Seller a one-time, non-refundable and non-creditable corresponding milestone payment (each, a "**Sales Milestone Payment**"). The [***] and the Earn-Out Report to be issued pursuant to Section 5.2.4 shall each indicate whether any Sales Milestone Event was achieved during the Calendar Quarter covered by such report. Upon receipt of an Earn-Out Report indicating that a Sales Milestone Event was achieved, Seller will issue an invoice to Buyer for the Sales Milestone Payment payable under this Section 5.4. Buyer will pay all Sales Milestone Payments payable under this Section 5.4 within [***] after receipt of such invoice. For the avoidance of doubt, each Sales Milestone Payment shall be payable one time upon the first achievement of the corresponding Sales Milestone Event, regardless of the number of times such Sales Milestone Event may be achieved.

TAK-228 Products Sales Milestones	
Sales Milestone Event	**Sales Milestone Payment**
Annual Net Sales of all TAK-228 Products equals or exceeds [***]	[***]
Annual Net Sales of all TAK-228 Products equals or exceeds [***]	[***]
Annual Net Sales of all TAK-228 Products equals or exceeds [***]	[***]
Annual Net Sales of all TAK-228 Products equals or exceeds [***]	[***]

TAK-659 Products Sales Milestones	
Sales Milestone Event	**Sales Milestone Payment**
Annual Net Sales of all TAK-659 Products equals or exceeds [***]	[***]
Annual Net Sales of all TAK-659 Products equals or exceeds [***]	[***]
Annual Net Sales of all TAK-659 Products equals or exceeds [***]	[***]
Annual Net Sales of all TAK-659 Products equals or exceeds [***]	[***]
Annual Net Sales of all TAK-659 Products equals or exceeds [***]	[***]

5.5 **Payments in Dollars**. All payments made by Buyer under this Article 5 shall be made by wire transfer from a banking institution in Dollars in accordance with instructions given in writing from time to time by Seller.

5.6 **Foreign Currency Exchange**. For the purpose of calculating any sums due under, or otherwise reimbursable pursuant to this Agreement (including the calculation of Net Sales) expressed in currencies other than Dollars, Buyer shall convert any amount expressed in a foreign currency into Dollar equivalents using the exchange rate used by Buyer in its financial reporting in accordance with U.S. GAAP.

5.7 **Overdue Payments**. Any amounts not paid by Buyer when due shall be subject to interest from and including the date payment is due, through and including the actual date of payment by Buyer, at a rate equal to the sum of (a) the prime rate of interest quoted in the *Wall Street Journal* (West Coast edition), plus (b) [***], calculated daily on the basis of a 365-day year, or if such edition is unavailable, a similar reputable data source.

5.8 **Taxes**.

5.8.1 **Taxes on Income**. Each Party shall be solely responsible for, and shall hold the other Party harmless in respect of, the payment of all Taxes, fees, duties, levies or similar amounts imposed on its share of income arising directly or indirectly from the activities of the Parties under this Agreement.

5.8.2 **Tax Withholding**. To the extent Buyer is required by applicable Law to deduct and withhold Taxes from the consideration otherwise payable pursuant to this Agreement to Seller, Buyer shall pay the amounts of such Taxes to the proper Governmental Entity in a timely manner and promptly transmit to Seller an official tax certificate or other evidence of such payment sufficient to enable Seller to claim such payment of Taxes within sixty (60) days following receipt of such evidence; provided, that prior to withholding any Taxes from consideration otherwise payable pursuant to this Agreement, Buyer shall use commercially reasonable efforts to notify Seller of the requirement to so withhold and to cooperate with Seller in Seller's reasonable efforts to eliminate, or mitigate, the amount of such withholding. To the extent that amounts are so withheld and paid to the proper Governmental Authority, such withheld amounts shall be treated for all purposes of this Agreement as having been paid to Seller.

5.8.3 **Redomicile, Assignment or Sublicense.** Notwithstanding anything in this Agreement to the contrary, the Parties acknowledge and agree that if either Party redomiciles, or assigns or sublicenses its rights or obligations under this Agreement (including an assignment of this Agreement as permitted under this Agreement), and such action leads to the imposition of Tax liability, including withholding or value added tax liability, on the other Party that would not have been imposed in the absence of such action or in an increase in such liability above the liability that would have been imposed in the absence of such action, then if such Party is Buyer, Buyer will increase such payment by the amount necessary to ensure that Seller receives an amount equal to the amount it would have received had no such action occurred.

5.8.4 **Transfer Taxes**. Unless otherwise agreed by the Parties in writing, the amounts payable under this Agreement are exclusive of all documentary, bulk transfer, sales or use, goods and services, value-added, gross receipts, stamp, registration or other similar transfer taxes, including all recording or filing fees, notarial fees and other similar costs, that may be imposed, payable, collectible or incurred in connection with the transfer and sale of the Acquired Assets as contemplated by the terms of this Agreement ("**Transfer Taxes**"). Such Transfer Taxes shall be borne [***]. Where such amounts are subject to Transfer Taxes, Seller shall promptly furnish Buyer with valid Tax invoices pursuant to applicable Law and remit the amounts of such Taxes to the proper Governmental Entity in a timely manner. Buyer shall settle all undisputed amounts, including any applicable Transfer Taxes, in accordance with Section 9.5.

5.8.5 **Tax Cooperation**. The Parties agree to cooperate with one another as may be reasonably necessary for the filing of Tax Returns, the making of any election with respect to Taxes, the preparation for any audit by any taxing authority and the prosecution or defense of any action relating to any Tax, and to use reasonable efforts to avoid or reduce Tax withholding, Transfer Taxes, or similar obligations in respect of the payments made by a Party under this Agreement, as permitted by applicable Law. On or prior to the Closing Date, Seller shall deliver to Buyer a properly completed IRS Form W-9 or applicable successor form.

5.8.6 **Allocation**. To the extent required for United States federal income Tax purposes, the Parties shall agree in good faith, within [***] after the Closing Date, on the manner in which the consideration referred to in Section 5.1 is to be allocated among the Acquired Assets (the "**Allocation Schedule**"). The Parties agree that the purchase price will be allocated among the assets of the Seller for

federal and state income Tax purposes in accordance with Section 1060 of the Internal Revenue Code of 1986, as amended (the "**Code**"), and the applicable regulations. No Party hereto shall file any Tax Return or other document with, or make any statement or declaration to, any governmental body that is inconsistent with the Allocation Schedule unless required to do so pursuant to a "determination" within the meaning of Section 1313 of the Code. Buyer and Seller also shall allocate and report any earn-out payments under Section 5.2, Development Milestone Payments or Sales Milestone Payments in accordance with the principles set forth in the Allocation Schedule as such payments are made and shall make appropriate adjustments to the Allocation Schedule.

5.8.7 **Personal Property Taxes**. All personal property Taxes and similar ad valorem Taxes levied with respect to the Acquired Assets for a Straddle Period shall be apportioned between Seller and Buyer as of the relevant Assignment Date based on the number of days of such taxable period included in the Pre-Closing Tax Period, and the number of days of such taxable period in the Post-Closing Tax Period. Seller shall be liable for the proportionate amount of such Taxes that is attributable to the Pre-Closing Tax Period, and Buyer shall be liable for the proportionate amount of such Taxes that is attributable to the Post-Closing Tax Period.

5.8.8 **Adjustment to Purchase Price.** Any payments made pursuant to Section 5.2, Section 5.3, Section 5.4 and Article 9 shall constitute an adjustment of the purchase price for Tax purposes and shall be treated as such by Buyer and Seller on their Tax Returns unless otherwise required pursuant to a "determination" within the meaning of Section 1313 of the Code.

5.9 **Mode of Payment**. All payments under this Agreement to Seller shall be made by deposit in the requisite amount to the bank account of Seller set forth in Schedule 5.9 or such other account as Seller may from time to time designate by written notice to Buyer.

ARTICLE 6.
REPRESENTATIONS AND WARRANTIES

6.1 **Representations and Warranties of Seller**. Seller represents and warrants to Buyer that the statements in this Section 6.1 are true, complete and correct as of the Closing Date, except as and to the extent set forth in Exhibit E (the "**Disclosure Schedule**"):

6.1.1 **Organization and Standing**. Seller is a corporation duly organized, validly existing and in good standing under the Laws of Delaware.

6.1.2 **Authorization**. Seller has all requisite power and authority to execute this Agreement, to carry out and perform its obligations under this Agreement and the Ancillary Agreements and to consummate the transactions contemplated hereunder and thereunder. The execution, delivery and performance by Seller of this Agreement and the Ancillary Agreements, and the consummation of the transactions contemplated hereunder and thereunder, have been duly and validly authorized by all necessary action of Seller.

6.1.3 **Binding Agreement**. This Agreement has been, and each of the Ancillary Agreements to which Seller is or will be a party, will be at the Closing, duly and validly executed and delivered on behalf of Seller and, assuming the due authorization, execution and delivery by Buyer, each such agreement constitutes the legal and binding obligation of Seller enforceable against Seller in accordance with its terms, subject to the effects of bankruptcy, insolvency, fraudulent conveyance, reorganization, moratorium and other similar laws relating to or affecting creditors' rights generally and to general equity principles (whether considered in a proceeding in equity or at law).

6.1.4 **Consents; No Violation, Etc**. The execution and delivery of this Agreement and the Ancillary Agreements do not, and the consummation of the transactions contemplated hereby and thereby will not (a) violate any Law applicable to Seller or its Affiliates, (b) conflict with any provision of the certificate of incorporation, bylaws or other organizational documents of Seller, or (c) give rise to any approval, authorization, consent, license, filing or registration with any Court or Governmental Entity or (d) violate any material Contract of Seller, or to which Seller is a party or subject to or by which it or any of its assets or properties is otherwise bound; *provided*, *however*, that no representation or warranty is made in the foregoing clause (a) or (d) with respect to matters that, individually or in the aggregate, would not result in a material adverse effect on the Acquired Assets or the transactions contemplated by this Agreement and the Ancillary Agreements.

6.1.5 **Title to Acquired Tangible Assets**. Seller and its Affiliates have good and valid title, right and interest to the portion of Acquired Assets that constitute tangible property, free and clear of all Encumbrances, other than Permitted Encumbrances.

6.1.6 **[***]**

6.1.7 **Brokers**. No broker, investment banker, financial advisor or other Person is entitled to any broker's, finder's, financial advisor's or similar fee or commission in connection with the transactions contemplated by this Agreement based upon arrangements made by or on behalf of Seller, except those for which Seller will be solely responsible.

6.1.8 **Intellectual Property**.

(a) Seller or its Affiliate is (a) the sole owner of the entire right, title and interest in and to the Assigned Patent Rights that are set forth on Schedule 1.1(h) – Part 1 as of the Closing Date and (b) the sole owner, or a joint owner with one or more Third Parties, of the entire right, title and interest in and to the Assigned Know-How, in each case free and clear of all Encumbrances, other than Permitted Encumbrances.

(b) None of the Assigned Patent Rights that are set forth on Schedule 1.1(h) – Part 1 as of the Closing Date has been finally adjudged invalid or unenforceable in whole or part, and, to Seller's Knowledge, all such Assigned Patent Rights are valid and enforceable. To Seller's Knowledge, all required filings and fees related to the Assigned Patent Rights that are set forth on Schedule 1.1(h) – Part 1 as of the Closing Date have been timely filed with and paid to the relevant Governmental Entity. [***]

(c) Except as set forth in any Assigned Agreement or Related Agreement, neither Seller nor any of its Affiliates has granted any Third Party any rights or authority with respect to any Assigned Intellectual Property.

(d) The Assigned Agreements are the only Contracts that Seller or its Affiliate is a party to prior to the Closing Date that include any royalty, license fee or other payment obligations with respect to the Programs for which Buyer will be liable following the Closing Date.

(e) To Seller's Knowledge, there is no unauthorized use, infringement or misappropriation of any of the Assigned Patent Rights that are set forth on Schedule 1.1(h) – Part 1 as of the Closing Date or material Assigned Know-How by any Third Party, including any current or former employee or consultant of Seller and its Affiliates.

(f) The Assigned Intellectual Property and the Patent Rights and Know-How licensed under the Assigned Agreements includes all Patent Rights and Know-How that are owned or in-licensed by Seller or its Affiliates and that relate solely to either or both of the Programs.

(g) [***].

6.1.9 **Assigned Agreements, Non-Assignable Contracts and Related Agreements**. Except as disclosed in Exhibit E, Seller has delivered to Buyer, prior to the date of this Agreement, true and complete copies of each Assigned Agreement, each Delayed Assigned Contract and each Non-Assignable Contract and Related Agreement that has been identified to the Knowledge of Seller as of the Closing Date. Each Assigned Agreement, Delayed Assigned Contract and Non-Assignable Contract is in full force and effect and valid and enforceable in accordance with its terms, except to the extent that any such agreement has expired in accordance with its terms and conditions (in which case the subject matter to be assigned or performed are the surviving rights and obligations thereunder). Except as disclosed in Exhibit E, neither the Seller nor the applicable Affiliate nor, to the Knowledge of Seller, any other party thereto is in default in the performance, observance or fulfillment of any obligation, covenant, condition or other term contained in any Assigned Agreement, Delayed Assigned Contract or Non-Assignable Contract, and the Seller or applicable Affiliate has not given or received written notice to or from any Person relating to any such alleged or potential default that has not been cured.

6.1.10 **Regulatory Documentation**. Seller has made available, or will make available as part of the transfer of Acquired Assets, to Buyer true and complete copies of, and the Regulatory Materials include, all registrations, applications, licenses, requests for approvals, exemptions, permits and other regulatory authorizations from the FDA or other Regulatory Authority related to the Program Molecules, Products and Programs, other than Regulatory Materials solely related to clinical trials of any Program Molecule or Product in combination with any Takeda Compound.

6.1.11 **Legal Compliance**. Seller and its Affiliates have conducted all research (excluding non-clinical research that was [***]) and development of Program Molecules and Products in compliance with all applicable Laws in all material respects. Seller and its Affiliates have not received any written communication from any Governmental Entity or any written notice, claim, request for information or complaint from any other Person alleging any failure to comply with or any liability under any applicable Laws relating to the Program Molecules, Products or Programs, and none is pending or, to Seller's Knowledge, threatened in writing.

6.1.12 **Existing Inventory**. The Existing Inventory has been stored in accordance with Seller's and its Affiliates' customary practices. Seller has provided Buyer true and complete copies of all batch records and quality documents related to the Existing Inventory.

6.1.13 **Taxes**.

(a) Seller is not a foreign person as that term is defined in Treasury Regulations Section 1.1445-2.

(b) There are no liens upon any of the Acquired Assets due to non-payment of Taxes or similar Tax-related matters, other than for Taxes not yet due and payable or that are being contested in good faith by appropriate proceedings, and no such liens will arise as a result of the execution of this Agreement and purchase of the Acquired Assets, other than in respect of Transfer Taxes borne by Buyer pursuant to Section 5.8.4.

6.2 **Representations and Warranties of Buyer**. Buyer represents and warrants to Seller that the statements in this Section 6.2 are true, complete and correct as of the Closing Date:

6.2.1 **Organization and Standing**. Buyer is a corporation duly organized, validly existing and in good standing under the laws of Delaware.

6.2.2 **Authorization**. Buyer has all requisite corporate power and authority to execute this Agreement and the Ancillary Agreements, to carry out and perform its obligations under this Agreement and the Ancillary Agreements and to consummate the transactions contemplated hereunder and thereunder. The execution, delivery and performance by Buyer of this Agreement and the Ancillary Agreements, and the consummation of the transactions contemplated hereunder and thereunder, have been duly and validly authorized by all necessary action of Buyer.

6.2.3 **Binding Agreement**. This Agreement has been, and each of the Ancillary Agreements to which Buyer is or will be a party, will be at the Closing, duly and validly executed and delivered on behalf of Buyer and, assuming the due authorization, execution and delivery by Seller, each such agreement constitutes the legal and binding obligation of Buyer enforceable against Buyer in accordance with their terms, subject to the effects of bankruptcy, insolvency, fraudulent conveyance, reorganization, moratorium and other similar laws relating to or affecting creditors' rights generally and to general equity principles (whether considered in a proceeding in equity or at law).

6.2.4 **Consents; No Violations, Etc**. The execution and delivery of this Agreement and the Ancillary Agreements do not, and the consummation of transactions contemplated hereby and thereby will not (a) violate any Law applicable to Buyer or its Affiliates, (b) conflict with any provision of the certificate of incorporation, bylaws or other organizational documents of Buyer, (c) give rise to any approval, authorization, consent, license, filing or registration with any Court or Governmental Entity or (d) violate any material Contract of, or to which Buyer is a party or subject to or by which it or any of its assets or properties is otherwise bound; *provided*, *however*, that no representation or warranty is made in the foregoing clauses (a) or (d) with respect to matters that, individually or in the aggregate, would not materially interfere with Buyer's performance of its obligations hereunder.

6.2.5 **HSR**. Buyer, or if different its Ultimate Parent Entity, has determined pursuant to 16 C.F.R. § 801.10 that the acquisition of the TAK-228 Program and TAK-659 Program do not satisfy the size of transaction jurisdictional test under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended ("**HSR Act**"). Unless otherwise defined, capitalized terms in this Section 6.2.5 have the meaning set forth in the HSR Act and related regulations.

6.2.6 **Financial Capability**. As of Closing, Buyer has available sufficient cash or other sources of immediately available funds to pay all upfront amounts payable pursuant to Section 5.1, and Buyer's obligations hereunder are not subject to any conditions regarding Buyer's ability to obtain financing for the transactions contemplated by this Agreement.

6.2.7 **Litigation**. As of the Closing Date, there is no Litigation pending or, to the knowledge of Buyer, threatened against Buyer or any of its Affiliates, which (a) challenges the transactions contemplated by this Agreement or the Ancillary Agreements, (b) if adversely determined, would delay the ability of Buyer to perform its obligations hereunder or (c) would have a material adverse effect on Buyer.

6.2.8 **No Brokers**. No broker, investment banker, financial advisor or other Person is entitled to any broker's, finder's, financial advisor's or similar fee or commission in connection

with the transactions contemplated by this Agreement based upon arrangements made by or on behalf of Buyer, except those for which Buyer will be solely responsible.

6.2.9 **Compliance**. Buyer will and it will ensure that its Affiliates, and require that its subcontractors and Licensees (including using commercially reasonable efforts to enforce applicable Contracts against subcontractors and Licensees), will conduct all activities relating to any Program and/or Product in compliance with applicable Law in all material respects, including applicable Law concerning data privacy and security (e.g., relating to medical records and medical information privacy that regulate or limit the maintenance, use, disclosure or transmission of medical records, patent information or other personal information).

6.2.10 **Adequacy of Information**. Buyer acknowledges and agrees that:

(a) other than the representations and warranties expressly set forth in Section 6.1, it has not relied on any representation or warranty made by Seller or any of its employees, agents, stockholders, Affiliates or representatives, express or implied, at Law or in equity, regarding the Programs, Products, the Acquired Assets or the subject matter of this Agreement;

(b) it will not assert any claim against Seller or any of its employees, agents, stockholders, Affiliates or any representatives or hold Seller or any such Persons liable for any inaccuracies, misstatements or omissions with respect to information furnished by Seller or any of its employees, agents, stockholders, Affiliates or any representatives, including any information in any "on-line" or physical data rooms or in any management presentations; and

(c) Seller makes no warranty with respect to the accuracy and completeness of any estimates, projections, forecasts, plans, budgets, future financial condition or any financial statements made available by Seller to Buyer.

For clarity, this Section 6.2.10 does not mitigate Seller's indemnification obligation pursuant to Article 9 for breach of representations and warranties expressly set forth in Section 6.1.

6.3 **Covenant of Buyer**. During the Term, Buyer will have available sufficient cash or other sources of immediately available funds to satisfy its diligence obligations pursuant to Section 3.2 and to pay all amounts payable pursuant to Article 5, including any Sales Milestone Payments, Development Milestone Payments and earn-out payments, in each case if, as and when due.

6.4 **No Other Warranties**. EXCEPT FOR THE REPRESENTATIONS AND WARRANTIES EXPRESSLY SET FORTH IN THIS ARTICLE 6, BOTH PARTIES DISCLAIM ALL OTHER REPRESENTATIONS AND WARRANTIES, EXPRESS OR IMPLIED, STATUTORY OR OTHERWISE, WITH REGARD TO THE PROGRAMS, PRODUCTS, THE ACQUIRED ASSETS AND THIS AGREEMENT, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, VALIDITY AND NON-INFRINGEMENT OF INTELLECTUAL PROPERTY RIGHTS.

ARTICLE 7.
CONFIDENTIALITY

7.1 **Confidentiality Obligations**. At all times during the Term, and for a period of [***] years thereafter, each Party shall, and shall cause its Affiliates, officers, directors, employees and agents to, keep confidential and not publish or otherwise disclose to a Third Party and not use, directly or indirectly, for any purpose, any Confidential Information furnished or otherwise made known to it, directly or

indirectly, by or on behalf of the other Party, except to the extent such disclosure or use is expressly permitted by the terms of this Agreement or is reasonably necessary or useful for the performance of such Party's obligations, or the exercise of such Party's rights, under this Agreement. "**Confidential Information**" of a Party means any technical, business, or other information provided by or on behalf of such Party to the other Party in connection with this Agreement, whether prior to, on, or after the Closing Date, including information relating to the terms of this Agreement, the Programs or Products (including the Acquired Assets), any research, development, making, having made, using, selling, offering for sale, and importing or other exploitation of the Program Molecules or Products; provided that (a) the terms of this Agreement will be deemed the Confidential Information of each Party, (b) any data from studies relating to a Program Molecule [***] will be deemed the Confidential Information of Seller, and (c) from and after the Closing Date, the Assigned Know-How and all information related solely to the Program Molecules, Products and Programs will be deemed, as between the Parties, the Confidential Information of Buyer and not of Seller, and Sections 7.1.2 and 7.1.4 will not apply with respect thereto. Each Party may disclose the other Party's Confidential Information for the purposes of performing its obligations or exercising its rights hereunder only to those of its and its Affiliates' employees, agents and contractors who require access thereto for the purpose of this Agreement and who are subject to written obligations of confidentiality and non-use with respect to such Confidential Information substantially similar to the obligations of confidentiality and non-use of the receiving Party pursuant to this Article 7. Notwithstanding the foregoing, the confidentiality and non-use obligations under this Section 7.1 with respect to any Confidential Information shall not include any information of the disclosing Party that:

7.1.1 is or hereafter becomes part of the public domain by public use, publication (including by a Third Party), general knowledge or the like through no wrongful act, fault or negligence on the part of the receiving Party in breach of this Agreement;

7.1.2 can be demonstrated by documentation or other competent proof to have been in the receiving Party's possession prior to disclosure by the disclosing Party without any obligation of confidentiality with respect to such information;

7.1.3 is subsequently received by the receiving Party from a Third Party lawfully in possession thereof who is not bound by any obligation of confidentiality with respect to such information; or

7.1.4 can be demonstrated by documentation or other competent evidence to have been independently developed by or for the receiving Party without reference to or use of the disclosing Party's Confidential Information.

Specific aspects or details of Confidential Information shall not be deemed to be within the public domain or in the possession of the receiving Party merely because the Confidential Information is embraced by more general information in the public domain or in the possession of the receiving Party. Further, any combination of Confidential Information shall not be considered in the public domain or in the possession of the receiving Party merely because individual elements of such Confidential Information are in the public domain or in the possession of the receiving Party unless the combination and its principles are in the public domain or in the possession of the receiving Party.

7.2 **Permitted Disclosures**. Notwithstanding anything to the contrary, Seller may disclose such Confidential Information that it deems necessary or desirable to comply with any disclosure or reporting obligations set forth in the Related Agreements, provided that each recipient is subject to written obligations of confidentiality and non-use with respect to such Confidential Information. In addition, each Party may disclose Confidential Information to the extent that such disclosure is:

7.2.1 made by or on behalf of Buyer to the Governmental Entities as required in connection with any filing, application or request for Regulatory Approval of a Product; *provided*, *however*, that reasonable measures shall be taken to assure confidential treatment of such information to the extent practicable and consistent with applicable Law;

7.2.2 made in response to a valid order of a court of competent jurisdiction or other supra-national, federal, national, regional, state, provincial and local governmental or regulatory body of competent jurisdiction or, if in the reasonable opinion of the receiving Party's legal counsel, such disclosure is otherwise required by applicable Law (including, for clarity, any disclosure required by applicable Law on clinicaltrials.gov or disclosure required by reason of filing with securities regulators, in which case, Section 7.4 shall also apply to such disclosure); *provided*, *however*, that to the extent practicable and not otherwise prohibited by applicable Law, the receiving Party shall first have given notice to the disclosing Party and given the disclosing Party (a) a reasonable opportunity to quash such order or to obtain a protective order or confidential treatment requiring that the Confidential Information and documents that are the subject of such order be held in confidence by such court or agency or, if disclosed, be used only for the purposes for which the order was issued and (b) a right to review and comment upon such disclosure, which comments shall be considered in good faith by the receiving Party; and *provided further* that the Confidential Information disclosed in response to such court or governmental order shall be limited to that information which is legally required to be disclosed in response to such court or governmental order;

7.2.3 made by or on behalf of Buyer or Seller to a patent authority as may be reasonably necessary or useful for purposes of obtaining or enforcing an Assigned Patent Right (in the case of Buyer) or [***] (in the case of Seller); *provided*, *however*, that reasonable measures shall be taken to assure confidential treatment of such information, to the extent such protection is available; or

7.2.4 made (a) by the receiving Party to its or its Affiliates' attorneys, auditors, advisors, consultants, contractors, existing or prospective acquirers, as may be necessary or useful in connection with the performance of its obligations or exercise of its rights as contemplated by this Agreement, or (b) by Buyer to existing or prospective collaboration partners, licensees, or other Third Parties, as may be necessary or useful in connection with the research, development, making, having made, using, selling, offering for sale, and importing or other exploitation of the Program Molecules or the Products; *provided*, *however*, that in each case (a) and (b) such persons shall be subject to written obligations of confidentiality and non-use with respect to such Confidential Information substantially similar to the obligations of confidentiality and non-use of the receiving Party pursuant to this Article 7 (with a duration of confidentiality and non-use obligations as appropriate that is no less than ten (10) years from the date of disclosure).

7.3 **Use of Name**. Except as expressly provided in this Agreement, neither Party shall mention or otherwise use the name, logo, or trademark of the other Party or any of its Affiliates (or any abbreviation or adaptation thereof) in any publication, press release, marketing and promotional material, or other form of publicity without the prior written approval of such other Party in each instance. The restrictions imposed by this Section 7.3 shall not prohibit either Party from making any disclosure identifying the other Party that is required by applicable Law.

7.4 **Public Announcements**.

7.4.1 Promptly following the Closing Date, Buyer may issue a press release announcing the transactions contemplated in this Agreement, which press release shall be in substantially the form of Exhibit D attached hereto, subject to any further changes that may be mutually agreed to by the Parties. Other than the press release described in the preceding sentence, neither Party shall issue any other public announcement, press release, or other public disclosure regarding this Agreement or its subject

matter without the other Party's prior written consent, except for any such disclosure that is, in the opinion of the disclosing Party's legal counsel, required by applicable Law or the rules of a stock exchange on which the securities of the disclosing Party or any of its Affiliates are listed (or to which an application for listing has been submitted). For clarity, the foregoing does not apply to public disclosures by Buyer regarding the plans for or results of its activities under this Agreement, which Buyer may make at its sole discretion without review or approval by Seller; provided, that Buyer shall not include in any press release, or otherwise publish or present on, any data, findings or results from studies relating to a Program Molecule in combination with a Takeda Compound or as the Parties may otherwise agree pursuant to Section 7.4.3.

7.4.2 In the event a Party or its Affiliates is, in the opinion of its legal counsel, required by applicable Law or the rules of a stock exchange on which its or its Affiliate's securities are listed (or to which an application for listing has been submitted) to make such a public disclosure, such Party shall submit the proposed disclosure in writing to the other Party as far in advance as reasonably practicable (and in no event less than [***] prior to the anticipated date of disclosure) so as to provide a reasonable opportunity to comment thereon; *provided, however*, if a Party or its Affiliates is required by applicable Law or the rules of a stock exchange to disclose this Agreement, such Party shall prepare a proposed redacted version of this Agreement, as applicable, to request confidential treatment for this Agreement, as applicable, and the other Party may promptly (and in any event, no less than [***] after receipt of such proposed redactions) provide its comments, which comments shall be considered in good faith and reasonably incorporated by the Party required to make such disclosure.

7.4.3 Subject to the prior review and written approval of Buyer, such approval not to be unreasonably withheld, delayed or conditioned, Seller may publish and present in scientific conferences or journals the result of Seller's development of Program Molecules conducted prior to the Closing Date. From time-to-time, the Parties may discuss in good faith any publications or presentations that Seller desires to publish or present (which shall be subject to the preceding sentence), such discussion to include the timing, content and venue of such proposed publications or presentations and any potential limitations on Buyer's public disclosure of data, findings or results to be included in such publications or presentations. Buyer shall not publicly disclose any draft publication or presentation provided by or on behalf of Seller to Buyer pursuant to this Section 7.4.3 in the form provided by Seller (or excerpts thereof) until publication or presentation thereof (and thereafter subject to any applicable limitations placed on such re-publication or re-presentation by the publishing journal).

ARTICLE 8.
TERM

8.1 **Term**. This Agreement shall commence on the Closing Date and shall continue in full force and effect until the earlier of (a) expiration of all obligations to make earn-out payments under Section 5.2 with respect to the last Product in all countries in the Territory or (b) termination by either Party pursuant to Section 8.2 (the "**Term**").

8.2 **Termination**.

8.2.1 **Termination for Material Breach**. Either Party (the "**Non-Breaching Party**") may terminate this Agreement in its entirety in the event the other Party (the "**Breaching Party**") has materially breached this Agreement, and such material breach has not been cured within [***] (or [***] in the case of an undisputed failure to make any payment due and payable under this Agreement) after receipt of written notice of such breach by the Breaching Party from the Non-Breaching Party (the "**Cure Period**"); provided that if the breach relates solely to TAK-228 Products or solely to TAK-659 Products, then the Non-Breaching Party will have the right to terminate this Agreement solely with respect to all TAK-228 Products or all TAK-659 Products, as applicable (such applicable Products, and the Program

Molecules within such Products, the "**Terminated Products**"), and will not have the right to terminate this Agreement in its entirety. The written notice describing the alleged material breach shall provide sufficient detail to put the Breaching Party on notice of such material breach. Any termination of this Agreement pursuant to this Section 8.2.1 shall immediately become effective at the end of the Cure Period, unless the Breaching Party has cured such material breach prior to the expiration of such Cure Period, or, if such material breach is not susceptible to cure within the Cure Period, then the Non-Breaching Party's right of termination shall be suspended only if and for so long as the Breaching Party provides to the Non-Breaching Party a written plan during the Cure Period that is reasonably calculated to effect a cure of such material breach, such plan is accepted by the Non-Breaching Party (such acceptance not to be unreasonably withheld, conditioned, or delayed), and the Breaching Party commits to and carries out such plan. [***]

8.2.2 **Termination for Bankruptcy**.

(a) Either Party may terminate this Agreement in its entirety upon providing written notice to the other Party if such other Party makes a general assignment for the benefit of creditors, files an insolvency petition in bankruptcy, petitions for or acquiesces in the appointment of any receiver, trustee or similar officer to liquidate or conserve its business or any substantial part of its assets, commences under the laws of any jurisdiction any proceeding involving its insolvency, bankruptcy, reorganization, adjustment of debt, dissolution, liquidation or any other similar proceeding for the release of financially distressed debtors, or becomes a party to any proceeding or action of the type described above, and such proceeding or action remains un-dismissed or un-stayed for a period of more than sixty (60) days.

(b) All rights and licenses granted under or pursuant to this Agreement are, and shall otherwise be deemed to be, for purposes of Section 365(n) of Title 11 of the United States Code and other similar laws in any jurisdiction outside the United States (collectively, the "**Bankruptcy Laws**"), licenses of rights to "intellectual property" as defined under the Bankruptcy Laws. If a case is commenced during the Term by or against a Party under Bankruptcy Laws then, unless and until this Agreement is rejected as provided pursuant to such Bankruptcy Laws, such Party (in any capacity, including debtor-in-possession) and its successors and assigns (including a Title 11 trustee) shall perform all of the obligations in this Agreement intended to be performed by such Party. If a case is commenced during the Term by or against a Party under the Bankruptcy Laws, this Agreement is rejected as provided for under the Bankruptcy Laws, and the non-bankrupt Party elects to retain its rights hereunder as provided for under the Bankruptcy Laws, then the Party subject to such case under the Bankruptcy Laws (in any capacity, including debtor-in-possession) and its successors and assigns (including a Title 11 trustee), shall provide to the non-bankrupt Party copies of all patent, Know-How and information necessary for the non-bankrupt Party to prosecute, maintain and enjoy its rights under the terms of this Agreement; provided that, to the extent applicable, the non-bankrupt Party continues to fulfill its payment obligations under Article 5 as specified herein in full. All rights, powers and remedies of the non-bankrupt Party as provided herein are in addition to and not in substitution for any and all other rights, powers and remedies now or hereafter existing at Law or in equity (including the Bankruptcy Laws) in the event of the commencement of a case by or against a Party under the Bankruptcy Laws. In particular, it is the intention and understanding of the Parties to this Agreement that the rights granted to the Parties under this Section 8.2.2(b) are essential to the Parties' respective businesses and the Parties acknowledge that damages are not an adequate remedy.

8.2.3 **Effects of Termination**. In the event of termination of this Agreement pursuant to Section 8.2.1 or 8.2.2 by either Party in its entirety (in which case all Program Molecules and Products will be considered Terminated Products) or with respect to certain Terminated Products:

(a) All rights and licenses granted to Buyer herein with respect to the Terminated Products shall terminate;

(b) At Seller's written request, Buyer shall assign to Seller the Acquired Assets and any Transaction IP Controlled by Seller that solely relates to, or was used by or on behalf of Buyer with respect to, the Terminated Products; and

(c) At Seller's written request, Buyer shall transfer to Seller any and all regulatory materials (including Regulatory Materials), including any INDs, Regulatory Filings or Regulatory Approvals, that are needed to continue fully exploiting the Terminated Products.

ARTICLE 9.
SURVIVAL; INDEMNIFICATION; INSURANCE; LIMITATIONS

9.1 **Survival of Representations, Warranties and Covenants**.

9.1.1 **Seller Representations**. The representations and warranties of Seller set forth in this Agreement shall survive the execution and delivery of this Agreement and the Closing Date and shall terminate at 11:59 PM Pacific Standard Time on the date that is [***] after the Closing Date, provided that the Fundamental Representations will survive for [***]. Notwithstanding the preceding sentence, any breach of a representation or warranty in respect of which indemnification may be sought under this Agreement shall survive the time at which it would otherwise terminate pursuant to the preceding sentence until the final resolution of such Claim (as defined below) if, prior to such time, both a Claim Certificate (as defined below) with respect to such breach shall have been timely delivered pursuant to Section 9.5 to Buyer and such Claim is pursued hereunder within a reasonable time period thereafter.

9.1.2 **Buyer Representations**. The representations and warranties of Buyer set forth in this Agreement shall survive the execution and delivery of this Agreement and the Closing Date and shall terminate at 11:59 PM Pacific Standard Time on the date that is [***] after the Closing Date. Notwithstanding the preceding sentence, any breach of a representation or warranty in respect of which indemnification may be sought under this Agreement shall survive the time at which it would otherwise terminate pursuant to the preceding sentence until the final resolution of such Claim if, prior to such time, both a Claim Certificate with respect to such breach shall have been timely delivered pursuant to Section 9.5 to Seller and such Claim is pursued hereunder within a reasonable time period thereafter.

9.1.3 **Covenants**. The respective covenants, agreements and obligations of Seller and Buyer set forth in this Agreement shall survive the execution and delivery of this Agreement and the Closing Date and shall terminate upon the earlier of (a) the expiration of the period explicitly set forth within such covenants, agreements and obligations (if any) and (b) expiration or earlier termination of this Agreement; provided that the rights and obligations of the Parties under Article 7 will remain in effect after expiration or termination of this Agreement for the time period set forth therein. Notwithstanding the preceding sentence, any breach of covenants, agreements and obligations in respect of which indemnification may be sought under this Agreement shall survive the time at which it would otherwise terminate pursuant to the preceding sentence until the final resolution of such Claim, if, prior to such time, both a Claim Certificate with respect to such breach shall have been timely delivered pursuant to Section 9.5 to the Party against whom such indemnification is sought and such Claim is pursued hereunder within a reasonable time period thereafter.

9.2 **Indemnification by Buyer**. Buyer agrees to defend Seller, its Affiliates and its (and its Affiliates') directors, officers, employees and agents (the "**Seller Indemnified Parties**") at Buyer's cost and expense, and will indemnify and hold Seller and the other Seller Indemnified Parties harmless from and against any claims, losses, costs, damages, Taxes (including penalties and interest), fees or expenses (including legal fees and expenses) (collectively, "**Losses**") resulting from any claims, actions or demands (collectively "**Claims**") arising out of or in connection with:

9.2.1 the breach by Buyer of this Agreement, including (a) any of the representations or warranties made hereunder by Buyer or (b) the covenants and obligations made hereunder by Buyer, including those related to the Assigned Agreements;

9.2.2 any Post-Closing Liabilities; and

9.2.3 the research, development, making, have made, use, sell, offer for sale, and import or otherwise exploitation of any Program or Product by or on behalf of Buyer or its Affiliates or (sub)licensees on or after the Closing Date, but only to the extent such Claim is brought by a Third Party against any Seller Indemnified Party(ies).

9.3 **Indemnification by Seller**. Seller agrees to defend Buyer, its Affiliates and its (and its Affiliates') directors, officers, employees and agents (the "**Buyer Indemnified Parties**") at Seller's cost and expense, and will indemnify and hold Buyer and the other Buyer Indemnified Parties harmless from and against any Losses resulting from any Claims arising out of or in connection with:

9.3.1 the breach by Seller of this Agreement, including (a) any of the representations or warranties made hereunder by Seller or (b) the covenants and obligations made hereunder by Seller;

9.3.2 any Excluded Liabilities; or

9.3.3 the research, development, making, have made, use, sell, offer for sale, and import or otherwise exploitation of any Program or Product by or on behalf of Seller or its Affiliates prior to the Closing Date, but only to the extent such Claim is brought by a Third Party against any Buyer Indemnified Party(ies).

9.4 **Limitations**.

9.4.1 **Deductible**. Subject to Section 9.4.4, no Claim may be made by any Indemnified Party for indemnification pursuant to Section 9.2 or Section 9.3 for breach of any representation or warranty in Article 6, but excluding any Fundamental Representations, until the aggregate amount of Losses for which an Indemnified Party seeks to be indemnified pursuant to Section 9.2 or Section 9.3, as the case may be, exceeds [***] (the "**Deductible**"), at which time the Indemnified Parties shall be entitled to indemnification for all such Losses in excess of the Deductible.

9.4.2 **Caps**. Subject to Section 9.4.4, the cumulative indemnification obligation of Seller under Section 9.3.1 shall not exceed [***].

9.4.3 **Calculation**. Any Losses as to which indemnification provided for in Section 9.2 or Section 9.3 may apply shall be determined net of any cash recovery actually received by an Indemnified Party with respect to insurance or other Third-Party recovery proceeds specifically with respect to the specific matter for which indemnification is sought, less any current costs associated with obtaining such recovery. If an Indemnified Party receives an indemnification payment pursuant to this Agreement and later receives insurance proceeds or other Third-Party recovery proceeds in respect of the related Losses, then the Indemnified Party shall promptly remit to the Indemnifying Party, amounts equal to the lesser of (a) the amount of such insurance proceeds or other Third-Party recovery proceeds, if any, and (b) the amount of the indemnification payment previously paid by or on behalf of the Indemnifying Party with respect to such Losses; *provided*, *however*, that the Indemnified Party shall not be obligated to pay such insurance proceeds or other Third-Party recovery proceeds in the event that the Indemnified Party has additional Losses which would have been recovered had such amounts been available from the

Indemnifying Party. This Section 9.4.3 shall not imply and shall not be construed to imply any obligation on the part of any Person to seek or pursue any such recovery and the failure to seek or pursue any such recovery shall not be defense to any indemnification obligation hereunder.

9.4.4 **Certain Exceptions to Limitations**. Notwithstanding anything to the contrary in this Agreement, the limitations and thresholds and other provisions set forth in this Article 9 shall not apply to Claims (a) involving fraud or (b) involving or related to any Sales Milestone Payments, Development Milestone Payments, earn-out payments or other payments payable by Buyer pursuant to this Agreement, and any Losses arising from or indemnification payments made on account of such Claims pursuant to this Article 9 shall not be taken into account in determining the applicability of such limitations and thresholds and other provisions to other Losses or Claims.

9.5 **Procedures**.

9.5.1 **General**. Promptly after the discovery by any Indemnified Party of any Loss or Losses, Claim or breach, including any Claim by a Third-Party (a "**Third-Party Claim**"), that would reasonably be expected to give rise to a Claim for indemnification hereunder, the Indemnified Party shall deliver to Seller or Buyer, whichever is the appropriate indemnifying party hereunder (the "**Indemnifying Party**"), a certificate (a "**Claim Certificate**") that:

(a) states that the Indemnified Party has paid or properly accrued Losses, or reasonably anticipates that it may or will incur liability for Losses, for which such Indemnified Party may be entitled to indemnification pursuant to this Agreement; and

(b) specifies in reasonable detail, to the extent practicable and available, each individual item of Loss included in the amount so stated, the basis for any anticipated liability and the nature of the misrepresentation, default, breach of warranty or breach of covenant or Claim to which each such item is related and, to the extent computable, an estimation of the amount to which such Indemnified Party claims to be entitled hereunder;

provided, *that* no delay on the part of any Indemnified Party in notifying the Indemnifying Party, shall relieve the Indemnifying Party of any liability or obligations hereunder except to the extent that the Indemnifying Party has been actually prejudiced thereby, and then only to such extent.

9.5.2 **Objection**. If the Indemnifying Party objects to the indemnification of an Indemnified Party in respect of any Claim or Claims specified in any Claim Certificate, the Indemnifying Party shall deliver a written notice to such effect to the Indemnified Party within [***] after the Indemnifying Party's receipt of such Claim Certificate. Thereafter, the Indemnifying Party and the Indemnified Party shall attempt in good faith to agree upon the rights of the respective parties for a period of not less than [***] after receipt by the Indemnified Party of such written objection with respect to each of such Claims to which the Indemnifying Party has objected. If the Indemnified Party and the Indemnifying Party agree with respect to any of such Claims, the Indemnified Party and the Indemnifying Party together shall promptly prepare and sign a memorandum setting forth such agreement. Should the Indemnified Party and the Indemnifying Party fail to agree as to any particular item or items or amount or amounts within such [***] period, then either party shall be entitled to pursue its available remedies for resolving its Claim for indemnification.

9.5.3 **Defense of Third-Party Claims**. The Indemnifying Party shall have the right to participate in, or by giving written notice to the Indemnified Party, to assume the defense of any Third-Party Claim at the Indemnifying Party's expense and by the Indemnifying Party's own legal counsel, and the Indemnified Party shall cooperate in good faith in such defense. In the event that the Indemnifying

Party assumes the defense of any Third-Party Claim, subject to Section 9.5.4, it shall have the right to take such action as it deems necessary to avoid, dispute, defend, appeal or make counterclaims pertaining to any such Third-Party Claim in the name and on behalf of the Indemnified Party. The Indemnified Party shall have the right to participate in the defense of any Third-Party Claim with legal counsel selected by it, subject to the Indemnifying Party's right to control the defense thereof. The fees and disbursements of such legal counsel shall be at the expense of the Indemnified Party. If the Indemnifying Party elects not to defend such Third-Party Claim, fails to promptly notify the Indemnified Party in writing of its election to defend as provided in this Agreement, or fails to diligently prosecute the defense of such Third-Party Claim, the Indemnified Party may, subject to Section 9.5.4, defend such Third-Party Claim and seek indemnification for any and all Losses based upon, arising from or relating to such Third-Party Claim (subject to the limitations set forth herein). Seller and Buyer shall cooperate with each other in all reasonable respects in connection with the defense of any Third-Party Claim, including making available records relating to such Third-Party Claim and furnishing, without expense (other than reimbursement of actual out-of-pocket expenses) to the defending party, management employees of the non-defending party as may be reasonably necessary for the preparation of the defense of such Third-Party Claim.

9.5.4 **Settlement of Third-Party Claims**. Notwithstanding any other provision of this Agreement, the Indemnifying Party may enter into settlement of any Third-Party Claim without the prior written consent of the Indemnified Party, except that the consent of the Indemnified Party, which will not be unreasonably withheld or delayed, shall be required to enter into any settlement of any such Third-Party Claim that commits the applicable Indemnified Party to take, or to forbear to take, any action or does not provide for a full and complete written release by the applicable Third Party of any applicable Indemnified Party. If the Indemnified Party has assumed the defense pursuant to Section 9.5.3, it shall not agree to any settlement without the written consent of the Indemnifying Party (which consent shall not be unreasonably withheld, conditioned or delayed).

9.5.5 **Agreed Claims**. Claims for Losses specified in any Claim Certificate to which the Indemnifying Party did not object in writing within thirty (30) days of receipt of such Claim Certificate, Claims covered by a memorandum of agreement of the nature described in Section 9.5.2 and claims for Losses the validity and amount of which have been the subject of resolution by arbitration or of a final non-appealable judicial determination are hereinafter referred to, collectively, as "**Agreed Claims**." The Indemnified Party shall be entitled to payment for any Agreed Claim within sixty (60) Business Days of the determination of the amount of any such Agreed Claims.

9.6 **Sole Remedy**. Other than rights and remedies provided in Section 9.4.4 and Section 10.12, the sole and exclusive remedy for any breach or alleged breach of any representation, warranty or covenant of this Agreement shall be indemnification in accordance with this Article 9.

9.7 **Insurance**. Buyer will obtain and maintain insurance for so long as it is developing or commercializing any Product, and for a period of at least [***] after the last commercial sale of any Product for any claims made policies, in an amount appropriate for its business and products of the type that are the subject of this Agreement and for its obligations under this Agreement. Specifically, Buyer will maintain (a) worker's compensation insurance with statutory limits in compliance with the worker's compensation laws of the state or states in which Buyer has employees in the United States (excluding Puerto Rico), (b) employer's liability coverage with a minimum limit of [***] per occurrence; provided that Buyer has employees in the United States (excluding Puerto Rico), (c) clinical trial insurance with a minimum limit of [***], and (d) general liability insurance with a minimum limit of [***] per occurrence and [***] in the aggregate, to be met by a combination of primary and excess limits. Beginning at least [***] prior to the initiation of a clinical trial involving any Product, Buyer will obtain and maintain clinical trial insurance (either separately or as part of the general or product liability insurance). Beginning at least [***] prior to the First Commercial Sale of a Product, Buyer will obtain and maintain product liability

insurance of [***]. Upon request, Buyer will provide Seller with evidence of the existence and maintenance of such insurance coverage. Buyer will notify Seller [***] in advance of cancelation of any such insurance. All such insurances under this Section 9.7 will be provided by a company or companies licensed to do business in United States having a financial rating of not less than A- Viii in the most current edition of Best's Key Rating Guide.

9.8 **LIMITATION OF DAMAGES**. IN NO EVENT SHALL EITHER PARTY BE LIABLE HEREUNDER TO THE OTHER PARTY FOR ANY PUNITIVE, RELIANCE, INDIRECT, SPECIAL, INCIDENTAL OR CONSEQUENTIAL DAMAGES (INCLUDING LOST REVENUE, LOST PROFITS, OR LOST SAVINGS) HOWEVER CAUSED AND UNDER ANY THEORY, EVEN IF IT HAS NOTICE OF THE POSSIBILITY OF SUCH DAMAGES. THE LIMITATIONS SET FORTH IN THIS SECTION 9.8 SHALL NOT APPLY WITH RESPECT TO (A) ANY BREACH OF ARTICLE 7 OR (B) THE WILLFUL MISCONDUCT, INTENTIONAL MISREPRESENTATION OR FRAUD OF A PARTY. NOTHING IN THIS SECTION 9.8 IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF A PARTY UNDER THIS ARTICLE 9 WITH RESPECT TO ANY DAMAGES PAID BY THE OTHER PARTY TO A THIRD PARTY IN CONNECTION WITH A THIRD-PARTY CLAIM.

ARTICLE 10.
MISCELLANEOUS

10.1 **Entire Agreement; Amendment**. This Agreement (including all Schedules and Exhibits attached to this Agreement) and the Ancillary Agreements constitute the entire agreement between the Parties as to the subject matter hereof. Except as set forth in this Section 10.1, (a) all prior and contemporaneous negotiations, representations, warranties, agreements, statements, promises and understandings with respect to the subject matter of this Agreement are hereby superseded and merged into, extinguished by and completely expressed by this Agreement and (b) neither Party shall be bound by or charged with any written or oral agreements, representations, warranties, statements, promises or understandings not specifically set forth in this Agreement. No amendment, supplement or other modification to any provision of this Agreement shall be binding unless in writing and signed by both Parties. Notwithstanding the foregoing, (i) all rights and obligations of the Parties that arose under the CDA during the period commencing on the CDA Effective Date and continuing through the Closing Date, including any dispute or alleged breach by a Party of any of the terms of the CDA during such period, shall be governed solely by the terms of the CDA, (ii) the terms and conditions of the CDA shall survive solely for the limited purposes set forth in subsection (i) above and (iii) the CDA shall otherwise terminate as of the Closing Date.

10.2 **Governing Law; Jurisdiction**. This Agreement and its effect are subject to and shall be construed and enforced in accordance with the law of the State of New York, without regard to its conflicts of laws that would require the application of any other Law. Each of the Parties hereby irrevocably and unconditionally consents to submit to the exclusive jurisdiction of the federal courts located in the Southern District of the State of New York for any matter arising out of or relating to this Agreement and the transactions contemplated hereby, and agrees not to commence any litigation relating thereto except in such courts. Each of the Parties hereby irrevocably and unconditionally waives any objection to the laying of venue of any matter arising out of this Agreement or the transactions contemplated hereby in the courts of the State of New York and hereby further irrevocably and unconditionally waives and agrees not to plead or claim in any such court that any such matter brought in any such court has been brought in an inconvenient forum. The Parties agree that a final judgment in any such matter shall be conclusive and may be enforced in other jurisdictions by suits on the judgment or in any other manner provided by law. Any proceeding brought by either Party under this Agreement shall be exclusively conducted in the English language.

10.3 **Waiver of Jury Trial**. To the fullest extent permitted by Law, each of the Parties irrevocably waives all right to trial by jury in any Litigation arising out of or relating to this Agreement or any of the transactions contemplated by this Agreement.

10.4 **Notice**. All notices or communication required or permitted to be given by either Party hereunder shall be deemed sufficiently given (a) three (3) Business Days after being sent by registered or certified mail, return receipt requested, postage prepaid, (b) one (1) Business Day after being sent for next Business Day delivery, fees prepaid, via a reputable nationwide overnight courier service or (c) on the date of confirmation of receipt (or the first Business Day following such receipt if the date of such receipt is not a Business Day) of transmission by email, in each case to the intended recipient as set forth below:

If to Buyer: [***]

With a copy to (which will not constitute notice):

[***]

If to Seller: [***]

Either Party may change the address to which notices and other communication hereunder are to be delivered by giving the other Party notice in the manner herein set forth.

10.5 **Compliance with Law; Severability**. Nothing in this Agreement shall be construed to require the commission of any act contrary to Law. If any one or more provisions of this Agreement is held to be invalid, illegal or unenforceable, the affected provisions of this Agreement shall be curtailed and limited only to the extent necessary to bring it within the applicable legal requirements and the validity, legality and enforceability of the remaining provisions of this Agreement shall not in any way be affected or impaired thereby.

10.6 **Successors and Assigns**. This Agreement shall bind and inure to the benefit of the successors and permitted assigns of the Parties hereto. Neither this Agreement nor any right, interest or obligation of a Party hereunder may be assigned by either Party without the written consent of the other Party, except that each Party may assign this Agreement and the rights, obligations and interests of such Party under this Agreement (a) in whole or in part, to any of its Affiliates, or (b) in whole, but not in part, in the event of a Change of Control of a Party; *provided, that*, (i) the assigning Party will provide the other Party with prompt written notice of assignment, (ii) the permitted assignee will assume all obligations of its assignor under this Agreement (or as related to the assigned part where a partial assignment to an Affiliate), (iii) unless expressly so agreed in writing by the Parties, no permitted assignment will relieve the assignor of liability under this Agreement, and (iv) any attempted assignment in contravention of this Section 10.6 shall be void.

10.7 **Waivers**. A Party's consent to or waiver, express or implied, of the other Party's breach of its obligations hereunder shall not be deemed to be or construed as a consent to or waiver of any other breach of the same or any other obligations of such breaching Party. A Party's failure to complain of any act, or failure to act, by the other Party, to declare the other Party in default, to insist upon the strict performance of any obligation or condition of this Agreement or to exercise any right or remedy consequent upon a breach thereof, no matter how long such failure continues, shall not constitute a waiver by such Party of its rights hereunder, of any such breach, or of any other obligation or condition. A Party's consent in any one instance shall not limit or waive the necessity to obtain such Party's consent in any future instance and in any event no consent or waiver shall be effective for any purpose hereunder unless such consent or waiver is in writing and signed by the Party granting such consent or waiver.

10.8 **Force Majeure**. Except for the obligation to pay money when due, neither Party shall be liable to the other for failure or delay in the performance of any of its obligations under this Agreement for the time and to the extent such failure or delay is caused by a Force Majeure. The Party affected by the Force Majeure shall provide the other Party in writing with full particulars thereof as soon as it becomes aware of the same (including its best estimate of the likely extent and duration of the interference with its activities), and will use commercially reasonable efforts to overcome the difficulties created thereby and to resume performance of its obligations as soon as practicable. For the avoidance of doubt, under no circumstances shall the alleged or actual inability to pay money be considered an event of Force Majeure.

10.9 **No Third Party Beneficiaries**. Nothing in this Agreement shall be construed as giving any Person, other than the Parties hereto and their successors and permitted assigns, any right, remedy or claim under or in respect of this Agreement or any provision hereof, except for the provisions of Article 9 (with respect to which the Persons to which Article 9 applies shall be Third Party beneficiaries in accordance with Article 9).

10.10 **Headings; Schedules and Exhibits**. Article and Section headings used herein are for convenient reference only, and are not a part of this Agreement. All Schedules and Exhibits are incorporated herein by this reference.

10.11 **Counterparts**. This Agreement may be executed in counterparts by a single Party, each of which when taken together shall constitute one and the same agreement. Counterparts may be delivered via facsimile, electronic mail (including .pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, Uniform Electronic Transactions Act or other applicable law) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

10.12 **Specific Performance**. The Parties agree that irreparable damage could occur if any provision of Article 7 of this Agreement were not performed in accordance with the terms thereof and that the Parties shall be entitled to seek specific performance of the terms of Article 7, without the necessity of posting a bond or other security or proving the inadequacy of damages as a remedy, in addition to any other remedy to which they are entitled at law or in equity.

10.13 **Further Assurances**. From time to time after the Closing Date, and for no further consideration (except as expressly set forth in Section 5.2, Section 5.3 and Section 5.4), each Party shall execute, acknowledge and deliver such assignments, transfers, consents, assumptions and other documents and instruments and take such other actions as may be necessary or desirable to consummate and make effective the transactions contemplated by this Agreement.

(Signature Pages Immediately to Follow)

IN WITNESS WHEREOF, this Agreement has been executed by the Parties hereto all as of the date first above written.

BUYER:

Calithera Biosciences, Inc.

By: /s/ Susan Molineaux
Name: Susan M. Molineaux
Title: President and Chief Executive Officer

SELLER:

Millennium Pharmaceuticals, Inc.

By: /s/ Nenad Grmusa
Name: Nenad Grmusa
Title: Head, Center for External Innovation

Schedule 1.1(a)

TAK-228 Structure

[***]

Schedule 1.1(b)

TAK-659 Structure

[***]

Schedule 1.1(c)

Materials

This section describes tangible assets to be transferred (excluding inventory and related manufacturing, controls and standards for testing).

[***]

Schedule 1.1(d)

Regulatory Materials

This section includes documentation related to regulatory submissions that is maintained in Takeda's EDMS (Electronic Document Management System) "Mosaic" and transition of open INDs and ODDs.

Additional regulatory submission documentation may be contained in Trial Master Files (TMFs; particularly for ex-US submissions (see Schedule 1.1(g)) and / or may be in paper files (see Schedule 1.1(g)).

[***]

Schedule 1.1(e)

Existing Inventory to be Transferred/Assigned

This section includes certain existing inventory of Drug substance and drug product (unlabeled and finished goods).

[***]

Schedule 1.1(f)

Assigned Agreements
[***]

Schedule 1.1(g)

Assigned Know-How

This Schedule includes intangible assets not described in other Schedules. Assigned Know-How is limited to the portions of the following intangible assets that are solely related to TAK-228 or TAK-659 and expressly excludes Know-How relating to a Program Molecule in combination with a Takeda Compound.

[***]

Schedule 1.1(h) – Part 1

Assigned Patent Rights

[***]

Schedule 1.1(h) – Part 2

In-Licensed Patent Rights

[***]

Schedule 1.1(i)

Initial Development Plan

[***]

Schedule 2.3

Acquired Assets

1. Assigned Intellectual Property
2. Regulatory Materials
3. Assigned Agreements
4. Materials
5. Existing Inventory to be Transferred/Assigned

Schedule 2.4

Select List of Excluded Assets

[***]

Schedule 2.6

Licensed Intellectual Property

[***]

Schedule 3.6

Related Agreements

[***]

Schedule 3.9

Delayed Assigned Contract

[***]

Schedule 5.9

Seller's Bank Account

[***]

Exhibit A

Form of Bill of Sale

This BILL OF SALE (this "**Agreement**") is made and entered into as of October 18, 2021, between Millennium Pharmaceuticals, Inc., a Delaware corporation ("**Seller**"), and Calithera Biosciences, Inc., a Delaware corporation, ("**Buyer**"). Capitalized terms used but not defined in this Agreement shall have the respective meanings set forth in the Purchase Agreement (as defined below).

WHEREAS, Seller and Buyer entered into that certain Asset Purchase Agreement, dated October 18, 2021 (the "**Purchase Agreement**"), which contemplates the sale by Seller to Buyer of the Acquired Assets; and

WHEREAS, in connection with the consummation of the transactions contemplated by the Purchase Agreement, Seller desires to assign its rights and obligations under the Acquired Assets to Buyer, and Buyer desires to accept such assignment and assume the obligations of Buyer under the Acquired Assets.

NOW, **THEREFORE**, in consideration of the premises and the mutual covenants, representations and warranties herein contained, and for other good and valuable consideration, the receipt and sufficiency of which are hereby mutually acknowledged, the Parties hereby agree as follows:

1. In accordance with the terms and subject to the conditions set forth in the Purchase Agreement (including Section 2.2.1 thereof), effective as of the Closing, the Seller hereby sells, conveys, transfers, assigns and delivers to, and hereby causes its Affiliates to sell, convey, assign, transfer and deliver to, Buyer all right, title, and interest, legal and equitable, of Seller and its Affiliates in and to all of the Acquired Assets, free and clear of any Encumbrance.

2. In accordance with the terms and subject to the conditions set forth in the Purchase Agreement (including Section 2.2.2 thereof), effective as of the Closing, the Buyer hereby accepts all right, title and interest, legal and equitable, in and to all of the Acquired Assets.

3. With regard to any Delayed Assigned Contract, the assignment of such Delayed Assigned Contract shall be effective as of the relevant Assignment Date.

4. This Agreement is being executed and delivered pursuant to, and is subject to and shall be governed by the terms and conditions of, the Purchase Agreement. Nothing in this Agreement is intended to or shall be deemed to amend, modify, supplement, or limit in any manner any of the representations, warranties, covenants, agreements, rights, or obligations of Seller and Buyer under the Purchase Agreement. In the event of any conflict between the terms and conditions of this Agreement and the terms and conditions of the Purchase Agreement, the terms and conditions of the Purchase Agreement shall control. This Agreement, the Purchase Agreement and the other Ancillary Agreements constitute the entire agreement between the Parties with respect to the subject matter hereof and thereof and supersede all prior agreements and understandings, both oral and written, between the Parties with respect to the subject matter hereof and thereof.

5. Any notice or other communication required or permitted under this Agreement shall be in writing and deemed to have been duly given if made in accordance with Section 10.4 (Notice) of the Purchase Agreement.

6. This Agreement shall bind and inure to the benefit of the successors and permitted assigns of the Parties; provided, that this Agreement may only be assigned in connection with a permissible assignment of the Purchase Agreement.

7. This Agreement hereby incorporates the provisions of Sections 10.2 (Governing Law; Jurisdiction) and 10.3 (Waiver of Jury Trial) of the Purchase Agreement, each of which shall apply to this Agreement as if fully set forth herein, *mutatis mutandis*.

8. Neither Party shall be bound by or charged with any written or oral agreements, representations, warranties, statements, promises or understandings not specifically set forth in this Agreement or the Purchase Agreement.

9. No amendment, supplement or other modification to any provision of this Agreement shall be binding unless in writing and signed by both Parties. A Party's consent to or waiver, express or implied, of the other Party's breach of its obligations hereunder shall not be deemed to be or construed as a consent to or waiver of any other breach of the same or any other obligations of such breaching Party. A Party's failure to complain of any act, or failure to act, by the other Party, to declare the other Party in default, to insist upon the strict performance of any obligation or condition of this Agreement or to exercise any right or remedy consequent upon a breach thereof, no matter how long such failure continues, shall not constitute a waiver by such Party of its rights hereunder, of any such breach, or of any other obligation or condition.

10. If any one or more provisions of this Agreement is held to be invalid, illegal or unenforceable, the affected provisions of this Agreement shall be curtailed and limited only to the extent necessary to bring it within the applicable legal requirements and the validity, legality and enforceability of the remaining provisions of this Agreement shall not in any way be affected or impaired thereby.

11. From time to time after the date of this Agreement, each Party shall execute, acknowledge and deliver such assignments, transfers, consents, assumptions and other documents and instruments and take such other actions as may be necessary or desirable to consummate and make effective the transactions contemplated by this Agreement.

12. This Agreement may be executed in counterparts by a single Party, each of which when taken together shall constitute one and the same agreement. Counterparts may be delivered via facsimile, electronic mail (including .pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, Uniform Electronic Transactions Act or other applicable law) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the parties have caused this Agreement to be executed and delivered as of the date first written above.

MILLENNIUM PHARMACEUTICALS, INC.

By: /s/ Nenad Grmusa
Name: Nenad Grmusa
Title: Head, Center for External Innovation

CALITHERA BIOSCIENCES, INC.

By: /s/ Susan Molineaux
Name: Susan M. Molineaux, Ph.D.
Title: President and Chief Executive Officer

Exhibit B

Form of Equity Agreement

See Exhibit 10.2

Exhibit C

Form of Patent Assignment Agreement

This PATENT ASSIGNMENT AGREEMENT (this "**Agreement**") is made and entered into as of October 18, 2021, between Takeda Pharmaceutical Company Limited, a company incorporated under the laws of Japan ("**Takeda**") and the parent of Millennium Pharmaceuticals, Inc. ("**Seller**"), and Calithera Biosciences, Inc., a Delaware corporation, ("**Buyer**"). Capitalized terms used but not defined in this Agreement shall have the respective meanings set forth in the Purchase Agreement (as defined below).

WHEREAS, Seller and Buyer entered into that certain Asset Purchase Agreement, dated October 18, 2021 (the "**Purchase Agreement**"), pursuant to which, among other things, Seller has agreed to enter into this Agreement (or to cause its Affiliate to enter into this Agreement) in order to assign to Buyer, Seller's and its Affiliates' right, title and interest to the Transferred Patent Rights (as defined below).

WHEREAS, in connection with the consummation of the transactions contemplated by the Purchase Agreement, Takeda, on behalf of itself and Seller, desires to assign its and its Affiliates' right, title and interest to the Transferred Patent Rights (as defined below) to Buyer, and Buyer desires to accept such assignment and assume the obligations of Buyer under the Transferred Patent Rights (as defined below).

NOW, **THEREFORE**, in consideration of the premises and the mutual covenants, representations and warranties herein contained, and for other good and valuable consideration, the receipt and sufficiency of which are hereby mutually acknowledged, the Parties hereby agree as follows:

1. In accordance with the terms and subject to the conditions set forth in the Purchase Agreement (including Sections 2.2.1(c) and 2.2.2(b) thereof), effective as of the Closing, Takeda on behalf of itself and Seller hereby sells, assigns, transfers, conveys and delivers to, and hereby causes its Affiliates to sell, convey, assign, transfer and deliver to, Buyer all of Takeda's and its Affiliates' (including Seller's) right, title and interest in and to those Patent Rights listed on Schedule 1 hereto, including the right to claim priority from the same in the United States and all foreign countries, and to claim the priority from the same as provided by the Paris Convention, together in each case with all registrations, applications therefor, patents (as applicable) issuing from any applications therefor, and renewals and extensions of the foregoing in the United States and for all foreign countries that are or may be secured under the laws of the United States and all foreign countries, including any division, renewal, continuation in whole or in part, substitution, conversion, reissue, reexamination, prolongation or extension thereof, now or hereafter in effect, for Buyer's own use and enjoyment as fully and entirely as the same would have been held and enjoyed by Takeda, Seller or any of their Affiliates if this assignment and sale had not been made, together with all income, royalties or payments due or payable as of the date of this Agreement or thereafter, including all claims for damages by reason of past, present or future infringement, misappropriation or other unauthorized use of such patents with the right to sue for and collect the same for Buyer's own use and enjoyment (collectively, the "**Transferred Patent Rights**"). Takeda on behalf of itself and its Affiliates hereby waives and agrees not to enforce any rights of attribution and integrity and other moral rights Takeda or any of its Affiliates may have in the Transferred Patent Rights.

2. Takeda on behalf of itself and its Affiliates hereby authorizes and requests the United States Commissioner of Patents and Trademarks and any other applicable government authority to record Buyer as the buyer and owner of the Transferred Patent Rights, and issue any and all registrations thereon to Buyer, as buyer of Seller's and its Affiliates' right, title and interest in, to and under the same, for the sole use and enjoyment of Buyer.

3. Following the date hereof, upon Buyer's reasonable request, and at Buyer's cost and expense, Takeda shall, and shall cause its Affiliates to, take such reasonable steps and actions, and provide such reasonable cooperation and assistance to Buyer and its successors, assigns, and legal representatives, including the execution and delivery of any affidavits, declarations, oaths, exhibits, assignments, or other documents, as may be reasonably necessary to effect, evidence or perfect the assignment of the Transferred Patent Rights to Buyer or any assignee or successor thereto.

4. This Agreement is being executed and delivered pursuant to, and is subject to and shall be governed by the terms and conditions of, the Purchase Agreement. Nothing in this Agreement is intended to or shall be deemed to amend, modify, supplement, or limit in any manner any of the representations, warranties, covenants, agreements, rights, or obligations of Seller and Buyer under the Purchase Agreement. In the event of any conflict between the terms and conditions of this Agreement and the terms and conditions of the Purchase Agreement, the terms and conditions of the Purchase Agreement shall control. This Agreement, the Purchase Agreement and the other Ancillary Agreements constitute the entire agreement between the parties hereto or thereto with respect to the subject matter hereof or thereof and supersede all prior agreements and understandings, both oral and written, between the parties hereto or thereto with respect to the subject matter hereof or thereof.

5. Any notice or other communication required or permitted under this Agreement shall be in writing and deemed to have been duly given if made in accordance with Section 10.4 (Notice) of the Purchase Agreement.

6. This Agreement shall bind and inure to the benefit of the successors and permitted assigns of the parties hereto; provided, that this Agreement may only be assigned in connection with a permissible assignment of the Purchase Agreement.

7. This Agreement hereby incorporates the provisions of Sections 10.2 (Governing Law; Jurisdiction) and 10.3 (Waiver of Jury Trial) of the Purchase Agreement, each of which shall apply to this Agreement as if fully set forth herein, *mutatis mutandis*.

8. Neither Party shall be bound by or charged with any written or oral agreements, representations, warranties, statements, promises or understandings not specifically set forth in this Agreement or in the Purchase Agreement.

9. No amendment, supplement or other modification to any provision of this Agreement shall be binding unless in writing and signed by both parties. A party's consent to or waiver, express or implied, of the other party's breach of its obligations hereunder shall not be deemed to be or construed as a consent to or waiver of any other breach of the same or any other obligations of such breaching party. A party's failure to complain of any act, or failure to act, by the other party, to declare the other Party in default, to insist upon the strict performance of any obligation or condition of this Agreement or to exercise any right or remedy consequent upon a breach thereof, no matter how long such failure continues, shall not constitute a waiver by such party of its rights hereunder, of any such breach, or of any other obligation or condition.

10. If any one or more provisions of this Agreement is held to be invalid, illegal or unenforceable, the affected provisions of this Agreement shall be curtailed and limited only to the extent necessary to bring it within the applicable legal requirements and the validity, legality and enforceability of the remaining provisions of this Agreement shall not in any way be affected or impaired thereby.

11. From time to time after the date of this Agreement, each party (and Seller or its Affiliates, as applicable) shall execute, acknowledge and deliver such assignments, transfers, consents, assumptions and other documents and instruments and take such other actions as may be necessary or desirable to consummate and make effective the transactions contemplated by this Agreement.

12. This Agreement may be executed in counterparts by a single party, each of which when taken together shall constitute one and the same agreement. Counterparts may be delivered via facsimile, electronic mail (including .pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, Uniform Electronic Transactions Act or other applicable law) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

[*SIGNATURE PAGE FOLLOWS*]

IN WITNESS WHEREOF, the undersigned have executed this Patent Assignment Agreement as of the date first set forth above.

TAKEDA PHARMACEUTICAL COMPANY LIMITED

By: /s/ Nenad Grmusa
Name: Nenad Grmusa
Title: Head, Center for External Innovation

CALITHERA BIOSCIENCES, INC.

By: /s/ Susan Molineaux
Name: Susan M. Molineaux, Ph. D.
Title: President and Chief Executive Officer

Schedule 1

Transferred Patent Rights

[***]

Exhibit D

Form of Press Release

Calithera Expands Oncology Pipeline with Acquisition of Two Clinical-Stage Assets from Takeda Pharmaceuticals

- *TORC 1/2 inhibitor sapanisertib and SYK inhibitor mivavotinib strengthen Company's precision oncology pipeline*
- *Calithera will initiate Phase 2 clinical trials of sapanisertib and mivavotinib in 2022*
- *Calithera to host webcast and conference call today at XX:XX a.m. ET / XX:XX a.m. PT*

SOUTH SAN FRANCISCO, Calif., October 18, 2021 (GLOBE NEWSWIRE) – Calithera Biosciences, Inc. (Nasdaq: CALA), a clinical-stage, precision oncology biopharmaceutical company, today announced an agreement with Takeda Pharmaceutical Company Limited ("Takeda") to acquire two clinical-stage compounds, both of which have demonstrated single-agent clinical activity with the greatest potential in biomarker-defined cancer-patient populations. The compounds, sapanisertib (CB-228, formerly TAK-228) and mivavotinib (CB-659, formerly TAK-659), further strengthen Calithera's pipeline of clinical-stage targeted therapies.

"We believe that these clinical-stage compounds are an excellent complement to our, internally-developed pipeline programs, and fit well with our current strategic focus on biomarker-driven therapeutic approaches. We are encouraged by the promising single-agent clinical data that suggest these investigational therapies could help to transform treatment for multiple cancer patient populations with high unmet need," said Susan Molineaux, PhD, president and chief executive officer of Calithera. "Specifically, sapanisertib has the potential to be the first targeted treatment for patients with NRF2-mutated squamous non-small cell lung cancer. We have learned a great deal about the unmet medical need of patients with KEAP1/NRF2 mutations and how to identify and recruit these patients during the conduct of our KEAPSAKE Trial, evaluating telaglenastat. This complementary approach in KEAP1/NRF2-mutant squamous NSCLC demonstrates our commitment to these patients and the pathway."

“Mivavotinib has the potential to be a best-in-class SYK inhibitor in non-Hodgkin’s lymphoma, as well as a first-to-market approach for patients with diffuse large B-cell lymphoma whose tumors harbor MyD88 and/or CD79 mutations.”

“We plan to start a clinical trial in squamous NSCLC with sapanisertib and a clinical trial in DLBCL with mivavotinib, both in biomarker specific populations, and generate data in the next twelve to eighteen months that will define the clinical development and potential regulatory approval paths for both of these compounds.”

The terms of the transaction include a total upfront cash payment to Takeda of $10 million and $35 million issued to Takeda in Calithera Series A preferred stock. Additionally, Takeda will be eligible to receive from Calithera clinical development, regulatory and sales milestone payments across both programs. Calithera will pay tiered royalties of high single-digits to low teens on future net sales should these candidates achieve regulatory approvals and subsequent commercial availability.

“Collaboration is an important aspect of our R&D strategy and at the center of our efforts to deliver new treatment options to patients. We are confident that Calithera, with their highly capable and experienced team, is the ideal partner to resume the development of sapanisertib and mivavotinib, and to maximize their potential to address underserved patient populations,” said Christopher Arendt, Ph.D., head of Oncology Cell Therapy and Therapeutic Area Unit of Takeda. “We look forward to seeing how these programs advance under Calithera’s leadership.”

Sapanisertib is a dual TORC 1/2 inhibitor that targets a key survival mechanism in KEAP1/NRF2-mutated tumor cells. These mutations are found in a considerable sub-population of patients across multiple solid tumor types. Sapanisertib has demonstrated promising single-agent activity in patients with relapsed/refractory NRF2-mutated squamous non-small cell lung cancer (NSCLC) and exhibits differential anti-tumor activity compared to rapalog inhibitors of TORC1 in NRF2-mutant squamous NSCLC *in vivo* models. A Phase 2 study planned to begin in the first quarter of 2022 will further evaluate sapanisertib as a monotherapy in patients with squamous NSCLC harboring a NRF2 mutation.

Mivavotinib is a SYK inhibitor that targets the constitutively active BCR pathway in many non-Hodgkin’s lymphoma (NHL) cases as well as the constitutively active inflammatory signaling pathway in MyD88 mutated NHL. In early phase studies, mivavotinib showed promising single-agent responses in relapsed/refractory diffuse large B-cell lymphoma (DLBCL). In addition, recent preclinical studies have shown enhanced SYK activity and sensitivity to SYK inhibition in DLBCL and other NHLs harboring

mutations in MyD88 and/or CD79, which comprises a distinct genetic subset of DLBCL known to have poor outcomes with standard of care therapy. Accordingly, Calithera plans to initiate a Phase 2 study of mivavotinib in 2022 for the treatment of patients with DLBCL with and without mutations in MyD88 and CD79. Beyond DLBCL, both preclinical and clinical data support expansion across additional NHL subtypes and other hematologic malignancies as part of long-term plans.

More information about sapanisertib and mivavotinib can be found at calithera.com/pipeline.

Webcast and Conference Call Information

Calithera will hold a webcast today, XXX, October X at XX:XX a.m./p.m. Eastern Time / XX:XX a.m./p.m. Pacific Time. To access the link to the webcast, which will be broadcast live in listen-only mode, or the subsequent archived recording, visit the Investors section of the Calithera website at www.calithera.com. Alternatively, the call may be accessed by dialing [INSERT] (domestic) or [INSERT] (international) and referring to conference ID [INSERT]. The webcast will be recorded and available for replay on Calithera's website for 30 days.

About Calithera

Calithera Biosciences 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 robust 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.

Calithera is headquartered in South San Francisco, California. For more information about Calithera, please visit www.calithera.com.

Forward Looking Statements
Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "may," "will," "expect," "anticipate," "estimate," "intend," "poised" and similar expressions (as well as other words or expressions referencing future events, conditions, or circumstances) are intended to identify forward-looking statements. These statements include those related to Calithera's clinical trials, the timing and enrollment of the KEAPSAKE, sapanisertib Phase 2 and mivavotinib Phase 2 trials,

the payment of future royalties, development, regulatory and sales milestone payments to Takeda, the potential impact and commercialization of sapanisertib for patients with NSCLC and a NRF2/KEAP1 mutation, the potential impact and commercialization of mivavotinib in patients with NHL with and without mutations in MyD88 and CD79. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. The potential product candidates that Calithera develops may not progress through clinical development or receive required regulatory approvals within expected timelines or at all. In addition, clinical trials may not confirm any safety, potency or other product characteristics described or assumed in this press release. Such product candidates may not be beneficial to patients or be successfully commercialized. The failure to meet expectations with respect to any of the foregoing matters may have a negative effect on Calithera's stock price. Additional information concerning these and other risk factors affecting Calithera's business can be found in Calithera's periodic filings with the Securities and Exchange Commission at www.sec.gov. These forward-looking statements are not guarantees of future performance and speak only as of the date hereof, and, except as required by law, Calithera disclaims any obligation to update these forward-looking statements to reflect future events or circumstances.

CONTACTS:

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Chief Financial Officer
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Media

Sam Brown, Inc.
Audra Friis
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audrafriis@sambrown.com

Investors

Burns McClellan
Lee Roth
212.213.0006
lroth@burnsmc.com

Exhibit E

Disclosure Schedules

- The following Non-Assignable Contracts and Related Agreements have not been disclosed to Buyer:
  [***]

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: November 9, 2021

/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: November 9, 2021

/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 September 30, 2021, 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: November 9, 2021

/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 September 30, 2021, 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: November 9, 2021

/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.