

Calithera Biosciences, Inc.
Form 10-Q
August 09, 2016

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 June 30, 2016

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
(State or other jurisdiction

27-2366329
(I.R.S. Employer

of incorporation or organization) Identification No.)

343 Oyster Point Blvd., Suite 200

South San Francisco, CA 94080

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(Address of principal executive offices including zip code)

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

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes ☒ No ☐

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

Large accelerated filer ☐

Accelerated filer ☒

Non-accelerated filer ☐ (do not check if a smaller reporting company) Smaller reporting company ☐

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 August 4, 2016, the registrant had 19,489,541 shares of common stock, \$0.0001 par value per share, outstanding.

Calithera Biosciences, Inc.

Quarterly Report on Form 10-Q

For the Quarter Ended June 30, 2016

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PART I. – FINANCIAL INFORMATION

Item 1. Financial Statements

Calithera Biosciences, Inc.

Condensed Balance Sheets

(Unaudited)

(In thousands, except per share amounts)

	June 30, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	\$7,326	\$6,105
Short-term investments	53,054	63,823
Prepaid expenses and other current assets	1,915	2,567
Total current assets	62,295	72,495
Long-term investments	-	1,997
Restricted cash	46	46
Property and equipment, net	854	931
Other assets	34	281
Total assets	\$63,229	\$75,750
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$1,446	\$562
Accrued liabilities	3,248	3,271
Total current liabilities	4,694	3,833
Deferred rent	316	129
Total liabilities	5,010	3,962
Commitments and contingencies		
Stockholders' equity:		
Common stock, \$0.0001 par value, 200,000 shares authorized		
as of June 30, 2016 and December 31, 2015;		
19,014 and 18,232 shares issued and outstanding as of		
June 30, 2016 and December 31, 2015, respectively	2	2
Additional paid-in capital	162,637	156,353
Accumulated deficit	(104,438)	(84,498)
Accumulated other comprehensive gain (loss)	18	(69)
Total stockholders' equity	58,219	71,788
Total liabilities and stock and stockholders' equity	\$63,229	\$75,750

See accompanying notes.

Calithera Biosciences, Inc.

Condensed Statements of Operations

(Unaudited)

(In thousands, except per share amounts)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Operating expenses:				
Research and development	\$7,776	\$5,533	\$14,842	\$11,163
General and administrative	2,665	2,341	5,256	4,578
Total operating expenses	10,441	7,874	20,098	15,741
Loss from operations	(10,441)	(7,874)	(20,098)	(15,741)
Interest income, net	83	56	158	65
Net loss	\$(10,358)	\$(7,818)	\$(19,940)	\$(15,676)
Net loss per share, basic and diluted	\$(0.55)	\$(0.44)	\$(1.07)	\$(0.87)
Weighted average common shares used to compute				
net loss per share, basic and diluted	18,987	17,963	18,688	17,955

See accompanying notes.

Calithera Biosciences, Inc.

Condensed Statements of Comprehensive Loss

(Unaudited)

(In thousands)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Net loss	\$(10,358)	\$(7,818)	\$(19,940)	\$(15,676)
Other comprehensive loss:				
Net unrealized gain (loss) on available-for-sale securities	14	(35)	87	(41)
Total comprehensive loss	\$(10,344)	\$(7,853)	\$(19,853)	(15,717)

See accompanying notes.

Calithera Biosciences, Inc.

Condensed Statements of Cash Flows

(Unaudited)

(In thousands)

	Six Months Ended June 30,	
	2016	2015
Cash Flows From Operating Activities		
Net loss	\$(19,940)	\$(15,676)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	152	228
Amortization of premiums on investments	343	112
Stock-based compensation	2,114	1,384
Gain on disposal of property and equipment	-	(8)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	618	194
Other assets	281	-
Accounts payable	884	230
Accrued liabilities	254	(21)
Deferred rent, non-current	46	(70)
Net cash used in operating activities	(15,248)	(13,627)
Cash Flows From Investing Activities		
Purchases of investments	(24,060)	(81,557)
Proceeds from sale or maturity of investments	36,570	4,536
Purchase of property and equipment	(211)	(285)
Net cash provided by (used in) investing activities	12,299	(77,306)
Cash Flows From Financing Activities		
Proceeds from issuance of common stock through an at-the-market offering, net	3,971	-
Proceeds from stock option exercises and employee stock plan purchases	199	283
Net cash provided by financing activities	4,170	283
Net increase (decrease) in cash and cash equivalents	1,221	(90,650)
Cash and cash equivalents at beginning of period	6,105	101,969
Cash and cash equivalents at end of period	\$7,326	\$11,319

See accompanying notes.

Calithera Biosciences, Inc.

Notes to Condensed Financial Statements

1. Organization and Basis of Presentation

Calithera Biosciences, Inc. (the “Company”) was incorporated in the State of Delaware on March 9, 2010. The Company is a clinical-stage biopharmaceutical company focused on discovering and developing novel small molecule drugs directed against tumor metabolism and tumor immunology targets for the treatment of cancer. The Company’s principal operations are based in South San Francisco, California, and it operates in one segment.

2. Summary of Significant Accounting Policies

Unaudited Interim Financial Information

The interim condensed balance sheet as of June 30, 2016, and the statements of operations, comprehensive loss, and cash flows for the six months ended June 30, 2016 and 2015 are unaudited. The unaudited interim 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 financial statements included in this report. The financial data and the other information disclosed in these notes to the financial statements related to the six-month periods are also unaudited. The results of operations for the six months ended June 30, 2016 are not necessarily indicative of the results to be expected for the year ending December 31, 2016 or for any other future annual or interim period. The balance sheet as of December 31, 2015 included herein was derived from the audited financial statements as of that date. These 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 (“SEC”).

Use of Estimates

The accompanying financial statements have been prepared in accordance with U.S. generally accepted accounting principles (“GAAP”). The preparation of 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 contingent assets and liabilities as of the date of the 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 preclinical, clinical trial and contract manufacturing accrued liabilities, fair value of common stock, 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.

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. Unrealized gains and losses are excluded from net loss 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 income, net in the statement of operations. The cost of securities sold is based on the specific-identification method. Interest on marketable securities is included in interest income, net.

Concentration 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.

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 include these costs in accrued liabilities in the balance sheets and within research and development expense in the 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.

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, 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.

Recent Accounting Pronouncements

In August 2014, the Financial Accounting Standards Board (the "FASB"), issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. ASU 2014-15 requires management to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. In doing so, companies will have reduced diversity in the timing and content of footnote disclosures than under today's guidance. ASU 2014-15 is effective for the Company for the 2016 annual period and with early adoption permitted. The Company will include the required disclosures in our December 31, 2016 annual financial statements to the extent that they are applicable.

In February 2016, the FASB issued ASU 2016-02, Leases. The ASU requires management to recognize lease assets and lease liabilities by lessees for all operating leases. The ASU is effective for the annual period beginning after December 15, 2018 and interim periods therein on a modified retrospective basis. The Company is currently assessing the impact the adoption of ASU 2016-02 will have on its financial statements.

In March 2016, the FASB issued ASU 2016-09, Compensation – Stock Compensation. ASU 2016-09 simplified certain aspects of the accounting for share-based payment transactions, including income taxes, classification of awards and classification in the statement of cash flows. ASU 2016-09 is effective for the annual period beginning after December 15, 2016, and interim periods therein. The Company is currently assessing the impact of adopting ASU 2016-09 will have on its financial statements.

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 financial statements on a recurring basis (at least annually). Financial instruments include cash and cash

equivalents, short-term investments, 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.

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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. There were no transfers between Level 1 and Level 2 during the periods presented.

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

June 30, 2016				
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	\$5,516	\$-	\$ -	\$5,516
Corporate notes and commercial paper	-	23,921	-	23,921
U.S. treasury securities	-	3,019	-	3,019
U.S. government agency securities	-	27,614	-	27,614
Total financial assets	\$5,516	\$54,554	\$ -	\$60,070

December 31, 2015				
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	\$5,548	\$-	\$ -	\$5,548
Corporate notes and commercial paper	-	23,151	-	23,151
U.S. treasury securities	-	4,329	-	4,329
U.S. government agency securities	-	38,340	-	38,340
Total financial assets	\$5,548	\$65,820	\$ -	\$71,368

4. Financial Instruments

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

June 30, 2016				December 31, 2015			
Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value	Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value

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Money market funds	\$5,516	\$ -	\$ -	5,516	\$5,548	\$ -	\$ -	5,548
Corporate notes and commercial paper	23,917	6	(2)	23,921	23,186	-	(35)	23,151
U.S. treasury securities	3,015	4	-	3,019	4,334	-	(5)	4,329
U.S. government agency securities	27,604	11	(1)	27,614	38,369	-	(29)	38,340
	\$60,052	\$ 21	\$ (3)	\$ 60,070	\$71,437	\$ -	\$ (69)	\$ 71,368
Classified as:								
Cash equivalents				\$ 6,970				\$ 5,502
Short-term investments				53,054				63,823
Long-term investments				-				1,997
Restricted cash				46				46
Total				\$ 60,070				\$ 71,368

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At June 30, 2016, 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 June 30, 2016, the Company had a total of \$60.4 million in cash, cash equivalents, and investments, which includes \$0.4 million in cash and \$60.0 million in cash equivalents and investments.

5. Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	June 30, 2016	December 31, 2015
Accrued bonus and payroll expenses	\$1,334	\$ 1,696
Accrued professional and consulting services	195	153
Accrued clinical and manufacturing expenses	1,434	921
Accrued preclinical and research expenses	137	194
Other	148	307
Total accrued liabilities	\$3,248	\$ 3,271

6. Stockholders' Equity

At-the-Market Offering

In November 2015, the Company entered into a sales agreement with Cowen and Company LLC ("Cowen"), as sales agent and underwriter, pursuant to which the Company may issue and sell shares of its common stock for an aggregate maximum offering price of \$50.0 million under an at-the-market ("ATM") offering program. The Company will pay Cowen up to 3% of gross proceeds for any common stock sold through the sales agreement.

During the six months ended June 30, 2016, the Company sold an aggregate of 715,383 shares of common stock pursuant to the ATM program, at an average price of approximately \$6.21 per share for gross proceeds of \$4.4 million, resulting in net proceeds of \$4.0 million after deducting underwriting fees and offering expenses. As of June 30, 2016, \$45.6 million of common stock remained available for sale under the ATM program.

7. Stock Based Compensation

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

Options Outstanding			
Number	Weighted-	Weighted-	Aggregate
of	Average	Average	Value
Shares	Exercise	Remaining	Intrinsic
Underlying			

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	Outstanding	Price	Contractual
	Options		Term
			(Years)
Outstanding — December 31, 2015	1,665	\$ 8.80	\$ 3,831
Options granted	935	\$ 4.78	
Options exercised	(17)	\$ 1.03	
Options canceled	(46)	\$ 6.74	
Outstanding — June 30, 2016	2,537	\$ 7.41	8.57 \$ 947

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

	Three Months		Six Months	
	Ended June		Ended June	
	30,		30,	
	2016	2015	2016	2015
Research and development	\$479	\$354	\$916	\$624
General and administrative	608	435	1,198	760
Total stock-based compensation	\$1,087	\$789	\$2,114	\$1,384

8. 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 per share attributable to common stockholders calculations because they would be anti-dilutive were as follows (in thousands):

	June 30,	
	2016	2015
Options to purchase common stock	2,537	1,872
Total	2,537	1,872

9. Licensing Agreements

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 ("Symbioscience License Agreement"). Under the terms of the Symbioscience License Agreement, the Company paid Symbioscience an upfront license fee of \$0.3 million in 2014 which was recorded in research and development expenses in the statement of operations. For the six months ended June 30, 2016 and 2015, the Company made milestone payments of \$0.2 million and \$0.2 million, respectively, which were recorded in research and development expenses in the statement of operations. No payments were made for the three months ended June 30, 2016 and 2015.

The Company may make future payments of up to \$24.0 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.

vTv License Agreement

In March 2015, the Company entered into a License and Research agreement with High Point Pharmaceuticals, LLC and TransTech Pharma LLC, or collectively TransTech, under which the Company obtained an exclusive, worldwide license to develop and commercialize TransTech's hexokinase II inhibitors ("vTv License Agreement"). The agreement was subsequently assigned by TransTech to its parent company, vTv Therapeutics LLC ("vTv"). Under the terms of the vTv License Agreement, the Company paid an initial license fee of \$0.6 million in 2015, which was recorded in research and development expense in the statement of operations. For the three and six months ended June 30, 2015, the Company recognized expense of \$0 million and \$0.6 million, respectively, which was recorded in research and development expense in the statement of operations. There were no expenses recorded in the three and six months

ended June 30, 2016.

The Company may pay potential development and regulatory milestone payments totaling up to \$30.5 million for the first licensed product. vTv is eligible for an additional \$77.0 million in potential sales-based milestones, as well as royalty payments, at mid-single digit royalty rates, based on tiered sales of the first commercialized licensed product. 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. The Company will be responsible for the worldwide development and commercialization of the licensed products, at its cost.

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 financial statements and related notes included in Part I, Item 1 of this report.

This discussion contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are identified by words such as “believe,” “will,” “may,” “estimate,” “continue,” “anticipate,” “intend,” “should,” “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.

Overview

We are a clinical-stage pharmaceutical company focused on discovering and developing novel small molecule oncology drugs directed against tumor and immune cell targets that control key metabolic pathways in the tumor microenvironment. Tumor metabolism and tumor immunology have emerged as promising new interrelated fields for cancer drug discovery, and recent clinical successes with therapeutic agents in each field have demonstrated the potential to create fundamentally new therapies for cancer patients. We are developing agents that take advantage of the unique metabolic requirements of tumor cells and cancer-fighting immune cells such as cytotoxic T-cells. Our lead product candidate, CB-839, is an internally discovered, first-in-class inhibitor of glutaminase, a critical enzyme in tumor cells. We are currently evaluating CB-839 in Phase 1 clinical trials in solid and hematological tumors. CB-839 administered as a single agent has resulted in clinical responses in renal cell cancer and acute myeloid leukemia, or AML, and clinical benefits in several other tumor types. We are currently enrolling patients in a series of combination Phase 1b cohorts in specific solid tumor types and AML. We are also planning to evaluate the immune-enhancing activity of CB-839 in a separate Phase 1/2 trial in the third quarter of 2016. We anticipate clinical updates in both renal cell carcinoma, or RCC, and triple negative breast cancer, or TNBC, in the fourth quarter of 2016. Our second product candidate, CB-1158, is a first-in-class immuno-oncology metabolic checkpoint inhibitor targeting arginase, an immunosuppressive enzyme in myeloid-derived suppressor cells responsible for T-cell suppression. In July 2016, we announced the acceptance of the Investigational New Drug application, or IND, by the U.S. Food and Drug Administration, or FDA. We intend to initiate a Phase 1 clinical trial with CB-1158 in the third quarter of 2016. We also have a third program directed towards the development of inhibitors of the tumor metabolism target hexokinase II and ongoing research efforts that are focused on discovering additional product candidates against novel tumor and immune cell metabolism targets.

Recent Developments

CB-839

Our lead product candidate, CB-839 is a potent, selective, reversible and orally bioavailable inhibitor of human glutaminase. CB-839 binds to a unique site on glutaminase that is distinct from the site that binds glutamine, thereby reducing the potential for undesirable side effects due to inhibition of other enzymes and receptors that bind glutamine. CB-839 takes advantage of the pronounced dependency many cancers have on the nutrient glutamine for growth and survival. In preclinical studies, CB-839 demonstrated broad antitumor activity in cell lines, inhibited the growth of human tumors in animal models, and was well tolerated in animals at doses above those shown to inhibit tumor growth. CB-839 was also synergistic with several approved cancer therapeutics that are part of the current standard of care.

The single agent safety and tolerability of CB-839 has been assessed in three Phase 1 clinical trials in patients with solid tumors, or CX-839-001, multiple myeloma or non-Hodgkin's lymphoma, or CX-839-002, and acute myeloid leukemia, CX-839-003. The optimal dose and schedule of single agent CB-839, 600-800 mg twice daily, or BID, with food, has been well tolerated across all three Phase 1 studies. An initial observation of Grade 3/4 increases in liver function enzymes was reduced to a rate of less than 2% with this regimen. Single agent objective responses have been observed in patients with metastatic renal cell cancer (a Partial Response, or PR), and acute myeloid leukemia (a Complete Response with incomplete recovery of peripheral blood counts, or CRi). Furthermore, 52% of patients with renal cell cancer have had stable disease or better, with several patients remaining on study. We have observed long lasting stable disease in renal cell cancer patients, ranging from 63 days to more than 17 months. These results were presented in November 2015 at the combined EORTC/NCI/AACR meeting and were updated at the 2016 American Society of Clinical Oncology, or ASCO, annual meeting in June.

In addition to single agent cohorts, we also initiated enrollment in six Phase 1b combination cohorts, one in which CB-839 is being combined with paclitaxel in patients with triple-negative breast cancer with everolimus (marketed as Afinitor) in renal cell cancer, or RCC, with erlotinib (marketed as Tarceva) in patients with EGFR-mutated non-small cell lung cancer, or NSCLC, with dexamethasone in patients with multiple myeloma, or MM, or with pomalidomide (marketed as Pomalyst) and dexamethasone in patients with multiple myeloma, and with azacitidine (marketed as Vidaza) in front-line AML.

Combination data from the Phase 1 solid tumor trial in RCC and TNBC were presented at the June 2016 ASCO meeting. Ten RCC patients, with a median of two prior therapies, were treated in combination with 10 mg daily everolimus. The overall disease control rate was 80%, including one partial response; among eight clear cell and papillary patients, the disease control rate was 100%. The median time on study for these patients was 6.5+ months, exceeding the expected progression free survival of everolimus alone in this population. Time on treatment was equal to, or greater than, the time on prior therapy for most patients, and seven of eight patients remained on study. The combination of CB-839 and everolimus has been well tolerated to date. There was one case of dose-limiting, grade 3 pruritic rash at the 400 mg dose level, which led to a reduction in the dose of everolimus for that patient.

Fifteen triple-negative breast cancer patients were treated with doses of CB-839 of 400, 600 or 800 mg twice daily in combination with 80 mg/m² IV paclitaxel, weekly, three weeks out of four. The majority of patients had received at least three prior lines of therapy. Six patients received five or more prior therapies in the advanced/metastatic setting. Most patients had received prior taxanes in either the neo-adjuvant (n=7) or metastatic (n=5) setting. Among patients treated with CB-839 doses of at least 600 mg (n=8), there were three partial responses (38%) and disease control (response or stable disease) in seven patients (88%). Two of the partial responses were observed in patients refractory to paclitaxel in a prior course of therapy. The combination of CB-839 and paclitaxel has been well tolerated to date, with adverse events that have been manageable and reversible. There was one case of dose-limiting, recurrent grade 3 neutropenia at the 400 mg dose level, which led to a reduction in the dose of paclitaxel for that patient.

In April 2016, we presented preclinical data at the American Association for Cancer Research, or AACR. We reported preclinical anti-tumor activity of CB-839 in combination with an anti-PD-L1 or an anti-PD-1 antibody. The combination of CB-839 and anti-PD-L1 or anti-PD-1 substantially increased the number of tumor regressions seen in the CT-26 syngeneic colon carcinoma model. Synergistic effects with CB-839 and anti-PD-L1 were also observed in a B16 melanoma model. We recently initiated a Phase 1/2 trial, CX-839-004, utilizing CB-839 in combination with nivolumab in patients with renal cell cancer, melanoma and non-small cell lung cancer. The Phase 1/2 study will assess the safety, pharmacokinetics and pharmacodynamics of CB-839 and nivolumab. We plan to enroll patients with clear cell renal cell carcinoma who are either naïve to checkpoint inhibitors, or were recently treated with nivolumab without tumor response, as well as melanoma and non-small cell lung cancer patients who have received anti-PD-1 monotherapy as their most recent line of therapy without tumor response.

Based on data generated from an academic research group at Case Western Reserve University, single agent CB-839 inhibits the growth of colorectal carcinomas with PIK3CA mutations in immunocompromised mice, but CRC tumors with a normal PIK3CA gene were not inhibited. These results have led to an investigator-sponsored trial at Case Western Reserve University which is planned to start in the second half of 2016 and will be enrolling colorectal cancer patients with a PIK3CA mutation for treatment with a combination of CB-839 and capecitabine.

Pending input from the FDA on the results of our Phase 1 trials, we plan to initiate one or more randomized, placebo-controlled Phase 2 clinical trials, likely in 2017, to study CB-839 in combination with approved conventional therapies and/or checkpoint inhibitors.

CB-1158

Our second product candidate, CB-1158, is an orally bioavailable inhibitor of arginase, an immunosuppressive enzyme in myeloid-derived suppressor cells responsible for T-cell suppression. Arginase depletes arginine, a nutrient

that is critical for the activation and proliferation of the body's cancer-fighting immune cells, such as cytotoxic T-cells and natural killer, or NK, -cells. During normal activation of the immune system, arginase, which is expressed by suppressive myeloid immune cells, plays an important role in halting T-cell proliferation. But in many tumors, including lung, gastrointestinal, bladder, renal cancer and acute myeloid leukemia, arginase-expressing myeloid cells accumulate and maintain an immunosuppressive environment, blocking the ability of T-cells and NK-cells to kill cancer cells. We believe that inhibitors of arginase can promote an anti-tumor immune response by restoring arginine levels, thereby allowing activation of the body's own immune cells, including cytotoxic T-cells and NK-cells.

In April 2016, we presented data at AACR which demonstrated that CB-1158 has single agent activity in animal models. Inhibition of tumor growth was accompanied by an increase in the local concentration of arginine, and the induction of multiple pro-inflammatory changes in the tumor microenvironment. CB-1158 increased CD8+ T-cell infiltrates in a lung tumor model. The addition of CB-1158 to anti-CTLA-4 and anti-PD-1, significantly inhibited tumor growth and reduced metastases in a mouse model that was resistant to dual checkpoint inhibitor therapy. CB-1158 was well tolerated as a single agent and in combination with checkpoint inhibitors in animal studies. We believe preclinical in vitro and in vivo data also predict good oral bioavailability of CB-1158 in humans. In July 2016, we announced the acceptance of the IND by the FDA. We intend to initiate a Phase 1 clinical trial with CB-1158 in the third quarter of 2016.

Critical Accounting Policies and Estimates

There have been no material changes in our critical accounting policies during the six months ended June 30, 2016, as compared to those disclosed in the Management’s Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates” in our Form 10-K dated December 31, 2015, 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. 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; and
- facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies;
- 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 six months ended June 30, 2016 and 2015:

	Three Months Ended June 30, 20162015 (in thousands)		Six Months Ended June 30, 20162015	
Development:				
CB-839 (Glutaminase inhibitor)	\$3,101	\$3,401	\$5,646	\$6,894
CB-1158 (Arginase inhibitor)	3,678	—	7,186	—
Total development	6,779	3,401	12,832	6,894
Preclinical and research:				

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Arginase inhibitors	—	1,982	722	3,401
Other preclinical and research	997	150	1,288	868
Total preclinical and research	997	2,132	2,010	4,269
Total Research and Development	\$7,776	\$5,533	\$14,842	\$11,163

We expect our research and development expenses will increase in the future as we advance our product candidates into and through clinical trials, pursue regulatory approval of our product candidates, which will require a significant investment in contract manufacturing and inventory build-up related costs.

We have exclusive license agreements with Mars, Inc., by and through its Mars Symbioscience division, to develop and commercialize their portfolio of arginase inhibitors and with High Point Pharmaceuticals, LLC and TransTech Pharma LLC, or collectively TransTech, (which was subsequently assigned by TransTech to its parent company, vTv Therapeutics LLC) to develop and commercialize their hexokinase II inhibitors. These license agreements will result in higher research and development expenses in the future.

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 trial enrollment, 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. 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 and amortization expense and other supplies. We expect to incur additional expenses as a public company, including expenses related to compliance with the rules and regulations of the SEC and those of the NASDAQ Global Select Market on which our securities are traded, and other administration and professional services.

Results of Operations

Comparison of the Three Months Ended June 30, 2016 and 2015

	Three Months Ended June 30,		Change	
	2016	2015	\$	%
	(in thousands, except percentages)			
Operating expenses:				
Research and development	\$7,776	\$5,533	\$2,243	41 %
General and administrative	2,665	2,341	324	14 %
Total operating expenses	10,441	7,874	2,567	33 %
Loss from operations	(10,441)	(7,874)	(2,567)	33 %
Interest income, net	83	56	27	*
Net loss	\$(10,358)	\$(7,818)	\$(2,540)	32 %

* Percentage not meaningful.

Research and Development. Research and development expenses increased \$2.2 million, or 41%, from \$5.5 million for the three months ended June 30, 2015 to \$7.8 million for the three months ended June 30, 2016. The increase of \$2.2 million was due to an increase of \$1.8 million primarily related to increased development activities in our arginase inhibitors program as we submitted an IND in June 2016, an increase of \$0.6 million in personnel-related costs primarily due to higher headcount, salary increases and stock-based compensation expense, offset by a decrease of \$0.2 million related to our licensing arrangements.

General and Administrative. General and administrative expenses increased \$0.3 million, or 14%, from \$2.3 million for the three months ended June 30, 2015 to \$2.7 million for the three months ended June 30, 2016. The increase of \$0.3 million was due to an increase of \$0.3 million in personnel-related costs as a result of higher headcount, salary

increases and stock-based compensation expense, an increase of \$0.2 million in professional services primarily related to higher legal costs associated with our in-licensing agreements, offset by a decrease of \$0.2 million for a payment to a third party related to a terminated license arrangement.

Interest Income. Interest income increased \$27,000, from \$56,000 for the three months ended June 30, 2015 to \$83,000 for the three months ended June 30, 2016. The increase of \$27,000 was primarily due to higher interest income generated from our cash equivalents and investment balances compared to the same period in the prior year.

Comparison of the Six Months Ended June 30, 2016 and 2015

	Six Months Ended June 30,		Change	
	2016	2015	\$	%
	(in thousands, except percentages)			
Operating expenses:				
Research and development	\$14,842	\$11,163	\$3,679	33%
General and administrative	5,256	4,578	678	15%
Total operating expenses	20,098	15,741	4,357	28%
Loss from operations	(20,098)	(15,741)	(4,357)	28%
Other income, net	158	65	93	*
Net loss	\$(19,940)	\$(15,676)	\$(4,264)	27%

* Percentage not meaningful.

Research and Development. Research and development expenses increased \$3.7 million, or 33%, from \$11.2 million for the six months ended June 30, 2015 to \$14.8 million for the six months ended June 30, 2016. The increase of \$3.7 million was due to an increase of \$3.1 million primarily related to increased development activities in our arginase inhibitors program as we submitted an IND in June 2016, an increase of \$1.2 million in personnel-related costs primarily due to higher headcount, salary increases and stock-based compensation expense, offset by a decrease of \$0.6 million related to our licensing arrangements.

General and Administrative. General and administrative expenses increased \$0.7 million, or 15%, from \$4.6 million for the six months ended June 30, 2015 to \$5.3 million for the six months ended June 30, 2016. The increase of \$0.7 million was due to an increase of \$0.7 million in personnel-related costs as a result of higher headcount, salary increases and stock-based compensation expense, an increase of \$0.1 million in professional services primarily related to higher legal costs associated with our in-licensing agreements, offset by a decrease of \$0.2 million for a payment to a third party related to a terminated license arrangement.

Interest Income. Interest income increased \$93,000, from \$65,000 for the six months ended June 30, 2015 to \$0.2 million for the six months ended June 30, 2016. The increase of \$93,000 was primarily due to higher interest income generated from our cash equivalents and investment balances compared to the same period in the prior year.

Liquidity and Capital Resources

As of June 30, 2016, we had cash, cash equivalents and investments totaling \$60.4 million. Our operations have been financed primarily by net proceeds from the sale of shares of our preferred stock, our initial public offering in October 2014 and our at-the-market, or ATM, offering program.

In November 2015, 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 \$150 million of our common stock. Up to \$50 million of the maximum aggregate offering price of \$150 million may be issued and sold pursuant to an ATM program under a sales agreement with Cowen and Company LLC, which is acting as our sales agent and underwriter. During the six months ended June 30, 2016, we sold an aggregate of 715,383 shares of common stock pursuant to the ATM program, at an average price of approximately \$6.21 per share for gross proceeds of \$4.4 million, resulting in net proceeds of \$4.0 million after deducting underwriting fees and offering expenses. As of June 30, 2016, \$145.6 million of our common stock remained available for sale pursuant to the shelf registration statement, of which \$45.6 million may be sold pursuant to the ATM program, subject to certain conditions as specified in the sales agreement.

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, cash equivalents and investments as of June 30, 2016 will be sufficient for us to meet our current operating plan for at least the next twelve months. 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. 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;

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- 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 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. 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:

	Six Months Ended June 30,	
	2016	2015
	(in thousands)	
Cash used in operating activities	\$(15,248)	\$(13,627)
Cash provided by (used in) investing activities	\$12,299	\$(77,306)
Cash provided by financing activities	\$4,170	\$283

Cash Flows from Operating Activities

Cash used in operating activities for the six months ended June 30, 2016 was \$15.2 million. Our net loss of \$19.9 million was offset in part by non-cash charges of \$2.1 million of stock-based compensation and \$0.5 million for depreciation and amortization. The change in operating assets and liabilities of \$2.1 million was primarily due to the timing of payments for our research and development activities.

Cash used in operating activities for the six months ended June 30, 2015 was \$13.6 million. Our net loss of \$15.7 million was offset in part by non-cash charges of \$0.2 million for depreciation and amortization and \$1.4 million of stock-based compensation. The change in operating assets and liabilities of \$0.3 million was primarily due to the

timing of payments for our clinical trials and manufacturing activities.

Cash Flows from Investing Activities

Cash provided by investing activities was \$12.3 million for the six months ended June 30, 2016 and was related to the sale or maturity of investments of \$36.6 million, offset by purchase of investments of \$24.1 million and purchase of property and equipment of \$0.2 million.

Cash used in investing activities was \$77.3 million for the six months ended June 30, 2015 and was related to the purchase of investments of \$81.6 million and purchase of property and equipment of \$0.3 million, partially offset by the sale or maturity of investments of \$4.5 million.

Cash Flows from Financing Activities

Cash provided by financing activities was \$4.2 million for the six months ended June 30, 2016 and was related to net proceeds from the issuance of common stock through our ATM program of \$4.0 million and issuance of common stock upon the exercise of stock options and employee stock plan purchases of \$0.2 million.

Cash provided by financing activities was \$0.3 million for the six months ended June 30, 2015 and was related to the issuance of common stock upon the exercise of stock options and employee stock plan purchases.

Contractual Obligations and Other Commitments

There have been no material changes to the contractual obligations during the three months ended June 30, 2016, as compared to those disclosed in our Annual Report on Form 10-K for the year ending December 31, 2015.

Off-Balance Sheet Arrangements

During 2015 and the three months ended June 30, 2016, we did not have any off balance sheet arrangements.

Recent Accounting Pronouncements

In August 2014, the Financial Accounting Standards Board, or FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. ASU 2014-15 requires management to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. In doing so, companies will have reduced diversity in the timing and content of footnote disclosures than under today's guidance. ASU 2014-15 is effective for the 2016 annual period and with early adoption permitted. We will include the required disclosures in our December 31, 2016 annual financial statements to the extent that they are applicable.

In February 2016, the FASB issued ASU 2016-02, Leases. The ASU requires management to recognize lease assets and lease liabilities by lessees for all operating leases. The ASU is effective for the annual period beginning after December 15, 2018 and interim periods therein on a modified retrospective basis. We are currently assessing the impact the adoption of ASU 2016-02 will have on our financial statements.

In March 2016, FASB issued ASU 2016-09, Compensation – Stock Compensation. ASU 2016-09 simplified certain aspects of the accounting for share-based payment transactions, including income taxes, classification of awards and classification in the statement of cash flows. ASU 2016-09 is effective for the annual period beginning after December 15, 2016, and interim periods therein. We are currently assessing the impact of adopting ASU 2016-09 will have on our financial statements.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. Our investment policy allows us to maintain a portfolio of cash equivalents and investments in a variety of 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. Our investment policy prohibits us from holding auction rate securities or derivative financial instruments. As of June 30, 2016, we had cash, cash equivalents and investments of \$60.4 million. A portion of our investments may be subject to interest rate risk and could fall in value if market interest rates increase. However, we believe that our exposure to interest rate risk is not significant as the majority of our investments are short-term in duration and a 1% change in interest rates would not have a significant impact on the total value of our portfolio. We actively monitor changes in interest rates. We had no outstanding debt as of June 30, 2016.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures.

Our management, with the participation of our President and Chief Executive Officer and our Chief Financial Officer, have evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) prior to the filing of this quarterly report. Based on that evaluation, our President and Chief Executive Officer and our Chief Financial Officer have concluded that, as of the end of the period covered by this quarterly report, 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 quarter to which this report relates that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

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

You should carefully consider the following risk factors, in addition to the other information contained in this report on Form 10-Q, including the section of this report titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and related notes. If any of the events described in the following risk factors and the risks described elsewhere in this report occurs, our business, operating results and financial condition could be harmed. This report on Form 10-Q also contains forward-looking statements that involve risks and uncertainties. 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 report. 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 June 30, 2016, except for those risks designated by an asterisk (*).

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 \$32.6 million and \$19.9 million for 2015 and the six months ended June 30, 2016, respectively. As of June 30, 2016, we had an accumulated deficit of \$104.4 million. To date, we have financed our operations primarily through private placements of our preferred stock, our initial public offering in October 2014 and our at-the-market program. We have devoted substantially all of our financial resources and efforts to research and development. We are currently in Phase 1 clinical trials on our lead product candidate, CB-839, and expect that it will 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 into and through clinical trials our existing clinical product candidates, CB-839, a glutaminase inhibitor for the treatment of solid and hematological tumors, and CB-1158, our arginase inhibitor;
- continue the preclinical development of our hexokinase II inhibitor program and advance a candidate into clinical trials;
- identify additional product candidates and advance them into preclinical development;
- 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;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel;
-

add operational, financial and management information systems and personnel, including personnel to support product development; and

· acquire or in-license other product candidates and technologies.

To become and remain profitable, we 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 and seek marketing approval for our product candidates, specifically CB-839 and CB-1158, and as we become obligated to make milestone payments pursuant to our outstanding license 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, preclinical development, laboratory testing and clinical trials for our product candidates, in particular CB-839 and CB-1158;
- the costs, timing and outcome of any regulatory review of our product candidate, CB-839 and CB-1158;
- the cost of our hexokinase II inhibitor program, and 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 marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- 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 we do not expect to be commercially available for many years, if at all.

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 collaborations, strategic alliances and licensing arrangements. We do not currently have any committed external source of funds. 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 collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or 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 clinical trials of our product candidate. We are currently evaluating CB-839 in Phase 1 clinical trials. In July

2016, we announced the acceptance of the IND application by the FDA. We intend to initiate a Phase 1 clinical trial with CB-1158 in the third quarter of 2016. 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, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors that may alter or delay our plans. We will need to transition from a company with a research focus to a company capable of supporting development activities and, if a product candidate is approved, a company with commercial activities. We may not be successful in any step in such a transition.

Risks Related to Drug Discovery, Development and Commercialization

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 and hexokinase 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 and hexokinase 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 and hexokinase 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.

We are very early in our development efforts, which may not be successful*.

We have invested a significant portion of our efforts and financial resources in the identification of our most advanced products candidate, CB-839, which is being evaluated in Phase 1 clinical trials. In July 2016, we announced the acceptance of the IND application by the FDA. We intend to initiate a Phase 1 clinical trial with CB-1158 in the third quarter of 2016. Our hexokinase II inhibitor program is in preclinical development. Because of the early stage of our development efforts and our unproven and novel approach to discovery and development of product candidates, we do not have a clearly defined clinical development path. It is also too early in our development efforts to determine whether our product candidates will demonstrate single-agent activity or will be developed for use in combination with other approved therapies, or both. 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 we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of CB-839 and CB-1158. The success of CB-839, CB-1158 and our hexokinase II inhibitor programs 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;

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- 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;
- launching commercial sales of the product candidates, if and when approved, whether alone or selectively in collaboration with others;
- 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; and
- enforcing and defending intellectual property rights and claims.

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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.

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.

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, 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
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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.

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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 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 physicians;
- 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 are currently evaluating CB-839 in Phase 1 clinical trials. In July 2016, we announced the acceptance of the IND application by the FDA. We intend to initiate a Phase 1 clinical trial with CB-1158 in the third quarter of 2016. All our other programs are in 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. 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 CB-839 and we have seen several adverse events deemed possibly or probably related to CB-839. As of [November 2015], a variety of adverse events, or AEs, have been reported. In the CX839-001 study, treatment-

emergent Grade ≥ 3 AEs occurring in $>5\%$ of patients included increases in liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT). With a change to twice daily dosing with food, only [one out of the 66] patients showed a Grade 3 liver enzyme increase. We have treated an insufficient number of patients to fully assess the safety of CB-839 and, as our trials progress, we may experience more frequent or more severe adverse events. Our ongoing and planned trials for CB-839 and CB-1158 may fail due to safety issues, and we may need to abandon development of CB-839 or CB-1158. Our hexokinase II inhibitor or 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.

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 in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

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

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, 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 physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

If, in the future, we are unable to establish 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 or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to other third parties. 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.

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 physicians or persuade adequate numbers of physicians 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. 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 physicians, 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.

There are also a number of product candidates in preclinical and clinical development by third parties to treat cancer by targeting cellular metabolism. Our principal competitors include Abbvie Inc., Advanced Cancer Therapeutics, LLC, Aeglea Biotherapeutics, Inc., Agios Pharmaceuticals, Inc., AstraZeneca plc, Bayer Pharma AG, Boehringer Ingelheim GmbH, Bristol-Myers Squibb Company, Celgene Corporation, Cornerstone Pharmaceuticals, Inc., CureTech Ltd., Eli Lilly and Company, Forma Therapeutics Holdings, LLC, Fortress Biotech, Inc., GlaxoSmithKline plc, Incyte Corporation, iTeos Therapeutics SA, Merck & Co., Janssen Biotech, Inc., Merck KGaA, NewLink Genetics Corporation, Novartis International AG, Ono Pharmaceuticals, Co., Ltd, Pfizer Inc., Quantum Pharmaceuticals, 3-V Biosciences, Inc., Regeneron Pharmaceuticals, Inc., Rhizen Pharmaceuticals SA, Roche Holdings, and its subsidiary Genentech Inc., Sanofi-Aventis Groupe, Sprint Biosciences, Takeda Pharmaceutical Co. Ltd. and TG Therapeutics, 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 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 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. Reimbursement may not be available for any product that we commercialize and, if reimbursement 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 reimbursement 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. 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.

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 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 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 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. 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 to do so 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 CB-839 and CB-1158 for our current and planned Phase 1 trials from third-party manufacturers. We have engaged third party manufacturers to obtain the active ingredient for CB-839 and CB-1158 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 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 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.

We may seek 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. 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.

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 a third party 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.

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To the extent we enter into any 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 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 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 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.
- 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 portfolios of arginase inhibitors and hexokinase II inhibitors, respectively, as part of our efforts to develop product candidates for these programs, and we are substantially dependent on these in-licenses for these programs. To the extent these in-licenses are terminated, our business may be harmed.

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 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.

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 are, 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

If we 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 physicians 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 postapproval 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.

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;