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

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 10-Q

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

343 Oyster Point Blvd., Suite 200

South San Francisco, CA 94080

(Address of principal executive offices including zip code)

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

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 x 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 x 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 x
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 x

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.

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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.

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

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

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 of Shares Underlying	Weighted-Average Exercise	Weighted-Average Remaining	Aggregate Value Intrinsic

	Outstanding Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
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 Ended June 30,		Six Months Ended June 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," "plan," "expect," "predict," "could," "potentially" or the negative of these terms or similar expressions. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other "forward-looking" information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in this report in Part II, Item 1A — "Risk Factors," and elsewhere in this report. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. These statements, like all statements in this report, speak only as of their date, and we undertake no obligation to update or revise these statements in light of future developments. We caution investors that our business and financial performance are subject to substantial risks and uncertainties.

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 pruitic 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 a 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,		Six Months Ended June 30,	
	2016	2015	2016	2015
	(in thousands)			
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:				

Arginase inhibitors	—	1,982	722	3,401
Other preclinical and research	997	150	1,288	868
Total preclinical and research	997			