Calithera Biosciences, Inc.
Form S-1/A
September 12, 2014
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As filed with the U.S. Securities and Exchange Commission on September 12, 2014.

Registration No. 333-198355

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT NO. 1

TO

FORM S-1

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

CALITHERA BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Delaware	**2834**	**27-2366329**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

343 Oyster Point Blvd. Suite 200

South San Francisco, California 94080

(650) 870-1000

(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

Susan M. Molineaux, Ph.D.

President and Chief Executive Officer

Calithera Biosciences, Inc.

343 Oyster Point Blvd. Suite 200

South San Francisco, California 94080

(650) 870-1000

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ¨

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

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. (Check one):

Large accelerated filer ¨	Accelerated filer ¨	Non-accelerated filer þ (Do not check if a smaller reporting company)	Smaller reporting company ¨

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED SEPTEMBER 12, 2014

PRELIMINARY PROSPECTUS

Shares

Common Stock

This is the initial public offering of shares of common stock of Calithera Biosciences, Inc.

We are offering shares of our common stock. Prior to this offering, there has been no public market for our common stock. We currently expect the initial public offering price to be between $ and $ per share of common stock. We have applied to list our common stock on the NASDAQ Global Market under the symbol CALA.

We are an emerging growth company under the federal securities laws and will be subject to reduced public company reporting requirements for this prospectus and future filings.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page 10.

	Per Share	Total

Initial public offering price	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds, before expenses, to us	$	$

(1) See Underwriting for additional disclosure regarding underwriting discounts, commissions and estimated offering expenses.

We have granted the underwriters the right to purchase up to additional shares of common stock to cover over-allotments, if any. The underwriters can exercise this right at any time within 30 days after the date of this prospectus.

The underwriters expect to deliver the shares against payment in New York, New York on or about , 2014.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Citigroup **Leerink Partners**

Wells Fargo Securities **JMP Securities**

, 2014

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We are responsible for the information contained in this prospectus and in any free writing prospectus we prepare or authorize. We have not, and the underwriters have not, authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the cover of this prospectus.

Persons who come into possession of this prospectus and any applicable free writing prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus and any such free writing prospectus applicable to that jurisdiction.

Until , 2014 (25 days after the date of this prospectus), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery is in addition to a dealer s obligation to deliver a prospectus when acting as an underwriter and with respect to their unsold allotments or subscriptions.

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SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary is not complete and may not contain all the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the risks of investing in our common stock discussed under the heading Risk Factors, and our financial statements and related notes included elsewhere in this prospectus before making an investment decision. Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to Calithera, the company, we, us and our refer to Calithera Biosciences, Inc.

Overview

We are a clinical-stage pharmaceutical company focused on discovering and developing novel small molecule drugs directed against tumor metabolism and tumor immunology targets for the treatment of cancer. Tumor metabolism and tumor immunology have emerged as promising new 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. Our lead product candidate, CB-839, is an internally discovered, first-in-class inhibitor of glutaminase, a critical enzyme in tumor metabolism. We are currently evaluating CB-839 in three Phase 1 clinical trials in solid and hematological tumors. Our lead preclinical program in tumor immunology is directed at developing inhibitors of the enzyme arginase and may provide a first-in-class therapeutic agent for this novel target. Our ongoing research efforts are focused on discovering additional product candidates against novel tumor metabolism and immunology targets.

The field of tumor metabolism seeks to exploit the unique ways in which cancer cells take up and utilize nutrients in order to grow and survive. It is now recognized that cancer cells rely on certain metabolic processes, or pathways, to a much greater extent than normal cells. The enhanced use of these pathways by cancer cells often results in a dependence on, or addiction to, these pathways that is not observed in normal cells. This creates an opportunity to selectively suppress the growth of cancer cells with therapeutic agents that specifically target these metabolic pathways.

Our lead product candidate in tumor metabolism, CB-839, takes advantage of the pronounced dependency many cancers have on the nutrient glutamine for growth and survival. CB-839 inhibits glutaminase, an enzyme required by cancer cells to utilize glutamine effectively. We are currently conducting three Phase 1 clinical trials of CB-839 in the United States in patients with solid tumors, leukemias, lymphomas and multiple myeloma. The purpose of these trials is to evaluate the safety of CB-839 both as a single agent and in combination with approved therapies and to seek preliminary evidence of efficacy. Pending input from the U.S. Food and Drug Administration, or FDA, on the results of our Phase 1 trials and our Phase 2 trial protocols, we plan to initiate one or more Phase 2 clinical trials of CB-839 in late 2015 or early 2016. We currently hold all commercial rights to CB-839.

The field of tumor immunology seeks to activate the body s own immune system to attack and kill cancer cells. Our preclinical program in tumor immunology is focused on developing selective inhibitors of the enzyme arginase. Arginase depletes arginine, a nutrient that is critical for the activation, growth and survival of the body s cancer-fighting immune 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 cancer-fighting immune cells. We are currently optimizing arginase inhibitors with the aim of submitting an Investigational New Drug, or IND, application to the FDA near the end of 2015.

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Our management team has considerable experience and success in the discovery and development of small molecule oncology drugs. Susan Molineaux, Ph.D., our Chief Executive Officer, was the founder and Chief Executive Officer of Proteolix, Inc., where she and several members of our current management team led the group that discovered and advanced through Phase 2 registration trials carfilzomib (marketed as Kyprolis), which was approved on an accelerated basis in 2012 for the treatment of refractory multiple myeloma. Additional members of our management team bring extensive experience in medicinal chemistry and in the financial management of private and public companies.

Our Strategy

Our goal is to build a leading independent biopharmaceutical company. We intend to leverage our expertise to discover, develop and commercialize cancer therapies targeting tumor metabolism and tumor immunology pathways to treat patients with unmet medical needs. Key elements of our strategy include:

Pursuing a broad clinical development program of CB-839 both as a single agent and in combination with approved therapies.

Identifying and pursuing efficient clinical development programs to enable rapid regulatory approval of CB-839.

Maximizing the commercial value of CB-839.

Advancing our first-in-class arginase inhibitor into clinical development.

Further developing our pipeline by leveraging our expertise in tumor biology, drug discovery and clinical development.

Our Research and Development Programs

The following table summarizes our ongoing and planned clinical trials from 2014 to 2016 for our lead programs in tumor metabolism and tumor immunology. We also intend to develop additional product candidates from our research and discovery efforts in these fields. In December 2013, we submitted two INDs to the FDA for CB-839, one for solid tumors and one for hematological tumors, covering each of the indications set forth in the table below.

Note: Phase 1 trials include a dose escalation stage followed by dose expansion in select tumor types.

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Our Lead Program in Tumor Metabolism: CB-839

CB-839 is an inhibitor of glutaminase, a tumor metabolism target that, based on our preclinical studies, is critical for the growth and survival of multiple tumor types. Due to CB-839 s novel mechanism of action, preclinical synergistic activity with existing cancer agents and favorable preclinical safety profile, we believe CB-839 has the potential to treat various cancers both as a single agent and in combination with approved therapies. We plan to pursue a broad development program for CB-839 focused on three distinct and significant opportunities:

- CB-839 as a single agent in cancers with large patient populations and significant unmet medical needs, such as triple-negative breast cancer and multiple myeloma.
- CB-839 in combination with standard of care drugs, initially with a cytotoxic agent for triple-negative breast cancer and an immunomodulatory agent for multiple myeloma.
- CB-839 as a single agent in rare tumors with identified driver mutations in metabolic enzymes where there is the potential for a rapid development pathway.

We believe this broad product development program provides the best opportunity to maximize the commercial value of CB-839.

In February 2014, we initiated three Phase 1 clinical trials in patients with solid tumors, leukemias, lymphomas and multiple myeloma to assess the safety and tolerability of CB-839. Each trial includes a dose escalation stage to identify the optimal dose for future clinical trials. Each trial will also have an expansion stage in which additional patients with specific tumor types will be enrolled to further evaluate the safety of CB-839 and to seek preliminary evidence of efficacy. During dose escalation, increased blood levels of CB-839 have been correlated with the inhibition of glutaminase and CB-839 has been generally well tolerated. As of July 25, 2014, 24 patients with cancers that had been heavily treated by other drugs had been enrolled in these trials, and 21 Grade 1 adverse events, or AEs, (most commonly nausea, vomiting and fatigue), two Grade 2 AEs and two Grade 3 AEs had been reported. Stable disease has been observed in several patients, including a TNBC patient who had a 13% decrease in tumor size after her third cycle of dosing with CB-839; she remains in the trial with no ongoing AEs. In addition to evaluating CB-839 as a single agent, we plan to enroll two Phase 1b combination cohorts, one in which CB-839 will be combined with paclitaxel in patients with triple-negative breast cancer and a second in which CB-839 will combined with pomalidomide (marketed as Pomalyst) and dexamethasone in patients with multiple myeloma. Pending input from the FDA on the results of our Phase 1 trials and our Phase 2 trial protocols, we plan to initiate in late 2015 or early 2016 one or more Phase 2 clinical trials to study CB-839 as a single agent or in combination with approved therapies.

Our Lead Program in Tumor Immunology: Arginase Inhibitors

Our preclinical program in tumor immunology is focused on developing selective arginase inhibitors. Arginase is an enzyme that depletes arginine, which is a naturally occurring amino acid that is critical for the activation, growth and survival of the body s cancer-fighting immune cells, known as cytotoxic T cells. Secreted arginase is present in patients with certain cancers, including renal cancer, acute myeloid leukemia and other tumor types, and may play an immunosuppressive role by blocking T cell activation. We believe that inhibitors of arginase can promote an anti-tumor immune response by restoring arginine levels, thereby allowing activation of the body s cytotoxic T cells. We are currently optimizing arginase inhibitors with the aim of submitting an IND application to the FDA near the end of 2015.

Risks Associated with our Business

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

- We have incurred significant operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future. We had an accumulated deficit of $39.8 million as of June 30, 2014.

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We will need substantial additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

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

Clinical trials of our product candidates will be costly and time consuming, and if they fail to demonstrate safety and efficacy to the satisfaction of the FDA, or similar regulatory authorities, we will be unable to commercialize our product candidates.

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.

If we are unable to obtain sufficient intellectual property protection or protect our intellectual property rights, our business may be harmed.

Healthcare policy and regulatory oversight in the United States and internationally are subject to rapid change, and if we are unable to respond, our business may be harmed.

We face substantial competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

If we are unable to adequately address these and other risks we face, our business, financial condition, operating results and prospects may be adversely affected.

In addition, we are an emerging growth company as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012, and therefore we intend to take advantage of certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, reduced disclosure obligations regarding executive compensation in this prospectus, our periodic reports and proxy statement and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments not previously approved. We may take advantage of these exemptions for up to five years or until we are no longer an emerging growth company.

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Corporate Information

We were incorporated in Delaware in March 2010 as Protein Activation Therapeutics, Inc. and subsequently changed our name to Calithera Biosciences, Inc. Our headquarters are located at 343 Oyster Point Blvd., Suite 200, South San Francisco, California 94080, and our telephone number is (650) 870-1000. Our website address is www.calithera.com. The information contained on, or that can be accessed through, our website is not part of, and is not incorporated by reference into this prospectus and should not be considered to be part of this prospectus. Investors should not rely on any such information in deciding whether to purchase our common stock.

Calithera, the Calithera logo and other trademarks or service marks of Calithera Biosciences, Inc. appearing in this prospectus are the property of Calithera Biosciences, Inc. Other trademarks, service marks or trade names appearing in this prospectus are the property of their respective owners. We do not intend our use or display of other companies trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

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The Offering

Common stock offered by us	shares
Common stock to be outstanding immediately after this offering	shares
Over-allotment option	shares
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $ million, or approximately $ million if the underwriters exercise in full their over-allotment option to purchase additional shares, at an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to further the clinical development of CB-839, further the development of our arginase inhibitor program, fund research and drug discovery activities related to additional product candidates, and for working capital and general corporate purposes. We may also use a portion of the net proceeds to acquire complementary businesses, products or technologies, although, we have no present commitments or agreements for any specific acquisitions.
Risk factors	You should read the section titled Risk Factors together with all the other information included in this prospectus before deciding to invest in shares of our common stock.
Proposed NASDAQ Global Market symbol	CALA

The number of shares of our common stock to be outstanding after this offering is based on 474,317,310 shares of common stock outstanding as of June 30, 2014, and exclude:

- 47,013,422 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2014 with a weighted-average exercise price of $0.04 per share, plus options to purchase an aggregate of 14,715,658 shares of common stock granted subsequent to June 30, 2014, with a weighted average exercise price of $0.14 per share;

- 2,021,776 shares of common stock reserved for future issuance under our 2010 Equity Incentive Plan as of June 30, 2014, plus an additional 21,078,262 shares of common stock reserved for future issuance subsequent to June 30, 2014, all of which shares will cease to be available for future issuance at the time our 2014 Equity Incentive Plan becomes effective in connection with this offering;

shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan, which will become effective upon the execution of the underwriting agreement related to this offering; and

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shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan, which will become effective upon the execution of the underwriting agreement related to this offering.

Unless otherwise noted, all information in this prospectus assumes:

a -for- reverse split of our common stock and preferred stock prior to the closing of this offering;

the conversion of all outstanding shares of preferred stock into 460,419,037 shares of common stock immediately upon the closing of this offering, which includes the conversion of the 91,324,195 shares of Series D preferred stock we issued and sold in July 2014;

that our amended and restated certificate of incorporation, which we will file in connection with the closing of this offering, and our amended and restated bylaws are effective;

no exercise of any outstanding options; and

no exercise of the underwriters over-allotment option to purchase additional shares.

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Summary Financial Data

The following tables summarize our financial data. We have derived the statements of operations data for the years ended December 31, 2012 and 2013 from our audited financial statements included elsewhere in this prospectus. The statements of operations data for the six months ended June 30, 2013 and 2014 and the balance sheet data as of June 30, 2014 are derived from our unaudited financial statements included elsewhere in this prospectus. We have prepared the unaudited financial statements on the same basis as the audited financial statements and have included, in our opinion, all adjustments, consisting only of normal recurring adjustments that we consider necessary for a fair presentation of the financial information set forth in those statements. Our historical results are not necessarily indicative of the results that may be expected in the future and results of interim periods are not necessarily indicative of the results for the entire year. You should read this data together with our financial statements and related notes, Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this prospectus.

	Years Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
			(unaudited)	
	(in thousands, except per share data)			
Statements of Operations Data:				
Operating expenses:				
Research and development	$ 6,558	$ 9,900	$ 4,069	$ 7,501
General and administrative	1,417	2,478	903	2,141
Total operating expenses	7,975	12,378	4,972	9,642
Loss from operations	(7,975)	(12,378)	(4,972)	(9,642)
Other income		1		2
Net loss	(7,975)	(12,377)	(4,972)	(9,640)
Gain on extinguishment of convertible preferred stock	2,889			
Net loss attributable to common stockholders	$ (5,086)	$ (12,377)	$ (4,972)	$ (9,640)
Net loss per share attributable to common stockholders, basic and diluted(1)	$ (7.63)	$ (2.74)	$ (1.76)	$ (0.98)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted(1)	667	4,517	2,820	9,816
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)(1)		$ (0.06)		$ (0.03)
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)(1)		195,982		378,910

(1) See Note 9 to our audited financial statements and Note 6 to our unaudited interim financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per common share, pro forma net loss per common share, and the weighted-average number of shares used in the computation of the per share amounts.

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	As of June 30, 2014		
	Actual	Pro Forma(1) (unaudited) (in thousands)	Pro Forma As Adjusted(2)(3)
Balance Sheet Data:			
Cash and cash equivalents	$ 27,750	$	$
Working capital	23,128		
Total assets	30,655		
Convertible preferred stock	54,282		
Accumulated deficit			