

Calithera Biosciences, Inc.
Form 424B5
August 18, 2017
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**Filed Pursuant to Rule 424(b)(5)
Registration No. 333-219791**

PROSPECTUS

\$50,000,000

Common Stock

We have entered into a sales agreement with Cowen and Company, LLC, or Cowen, relating to shares of our common stock, par value \$0.0001 per share, offered by this prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$50,000,000 from time to time through Cowen, acting as our agent.

Our common stock is listed on the NASDAQ Global Select Market under the symbol CALA. On August 17, 2017, the last reported sale price of our common stock on the NASDAQ Global Select Market was \$13.95 per share.

Sales of our common stock, if any, under this prospectus will be made in sales deemed to be at the market offerings as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act. Cowen is not required to sell any specific amount of securities, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Cowen and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Cowen for sales of common stock sold pursuant to the sales agreement will be an amount up to 3% of the gross proceeds of any shares of common stock sold under the sales agreement. In connection with the sale of the common stock on our behalf, Cowen will be deemed to be an underwriter within the meaning of the Securities Act and the compensation of Cowen will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cowen with respect to certain liabilities, including liabilities under the Securities Act or the Exchange Act of 1934, as amended.

Our business and an investment in our common stock involve significant risks. These risks are described under the caption Risk Factors beginning on page 8 of this prospectus and in the documents incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

Cowen

August 18, 2017

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we have filed with the Securities and Exchange Commission, or the SEC, utilizing a shelf registration process. Under the shelf registration process, we may offer shares of our common stock having an aggregate offering price of up to \$250,000,000. Under this prospectus, we may offer shares of our common stock having an aggregate offering price of up to \$50,000,000 from time to time at prices and on terms to be determined by market conditions at the time of offering.

Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus and all of the information incorporated by reference herein and therein, as well as the additional information described under the sections titled *Where You Can Find More Information* and *Incorporation of Documents by Reference*. These documents contain important information that you should consider when making your investment decision.

We provide information to you about this offering of shares of our common stock in this prospectus, which describes the specific details regarding this offering. If information in this prospectus is inconsistent with documents incorporated by reference in this prospectus filed prior to the date of this prospectus, you should rely on this prospectus. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in this prospectus the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates.

You should rely only on the information contained in this prospectus or in any free writing prospectus prepared by us or on our behalf. We have not, and Cowen has not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and Cowen is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that

date.

Information contained on our website is not part of this prospectus. We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are

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permitted. The distribution of this prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus outside the United States. This prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

INDUSTRY AND MARKET DATA

We obtained the industry and market data in this prospectus and the documents incorporated by reference herein from our own research as well as from industry and general publications, surveys and studies conducted by third parties. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the industry in which we operate is necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section titled **Risk Factors** and elsewhere in this prospectus. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

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PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference in this prospectus, and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus and any related free writing prospectus, including the risks of investing in our securities discussed under the section titled Risk Factors contained in this prospectus and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Calithera Biosciences, Inc.

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 immuno-oncology (I-O) 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. 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 oral inhibitor of glutaminase, a critical enzyme in tumor cells. CB-839 administered as a single agent has resulted in clinical responses in renal cell cancer and acute myeloid leukemia. We are currently enrolling patients in a randomized, double blind, placebo controlled Phase 2 trial in renal cell carcinoma (RCC) and a Phase 2 trial in triple negative breast cancer (TNBC). We are also enrolling patients in a series of combination Phase 1/2 cohorts in specific solid tumor types including a trial in combination with cabozantinib in RCC patients, and a trial in combination with nivolumab in RCC, melanoma and non-small cell lung cancer patients. CB-839 has been very well tolerated both as a single agent and in combination with other therapies. Our second product candidate, CB-1158, is a first-in-class oral inhibitor of arginase, an enzyme that depletes the amino acid arginine, a key metabolic nutrient for T-cells, and is being co-developed with Incyte Corporation (Incyte) for hematology and oncology indications. CB-1158, also known as INCB001158, is currently being tested in a Phase 1 clinical trial in patients with solid tumors as a single agent and in combination with a PD-1 inhibitor. We also have ongoing research efforts that are focused on discovering additional product candidates against novel tumor metabolism and immunology targets.

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. In preclinical studies, CB-839 demonstrated broad antitumor activity in tumor cell lines, inhibited the growth of human tumors in animal models and was well tolerated in toxicity studies. CB-839 was also synergistic with several approved, standard of care, cancer therapeutics. We believe CB-839 has the potential to be an important new therapeutic agent with a novel mechanism of action for the treatment of a broad range of cancers, and is the only selective glutaminase inhibitor currently in clinical trials. We currently retain all commercial rights to CB-839 and have been granted a U.S. patent, which includes composition of matter coverage for CB-839, through 2032.

CB-839 may also have the potential to work in combination with immuno-oncology therapeutics. Inhibition of glutaminase results in accumulation of glutamine, the substrate of glutaminase, in tumors.

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Glutamine, which is frequently depleted in the tumor microenvironment due to avid uptake by tumor cells, has been shown to be an important nutrient for T-cell proliferation. Administration of CB-839 to tumor-bearing animals substantially enhances the anti-tumor activity of checkpoint inhibitors, potentially by restoring the levels of glutamine in the tumor microenvironment and thereby enabling T-cells to proliferate. Checkpoint inhibitors, including the approved agents nivolumab (marketed as Opdivo) and pembrolizumab (marketed as Keytruda), are a class of immuno-oncology agents directed against programmed death protein-1 (PD-1) or programmed death ligand-1 (PD-L1) that promote the activation and tumor-killing properties of the patient's own immune cells, such as cytotoxic T-cells. CB-839 could potentially have multiple mechanisms of action in the treatment of cancer first by starving the tumor cell, and second by facilitating the activation of T-cells in the nutrient-deprived tumor microenvironment.

CB-1158 is a potent and selective orally bioavailable inhibitor of the enzyme arginase that was discovered at Calithera and is being co-developed with Incyte. 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 (NK)-cells. During normal activation of the immune system, arginase, which is expressed by myeloid immune cells known as myeloid-derived suppressor cells (MDSCs), 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.

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.

Renal Cell Carcinoma

CB-839 is being developed for the treatment of patients with RCC. In 2017, RCC is estimated to be diagnosed in 63,990 people in the United States, according to the National Cancer Institute. We evaluated CB-839 as a monotherapy in a RCC cohort in the dose expansion stage of our solid tumor Phase 1 clinical trial CX-839-001. As of December 31, 2016, 20 efficacy-evaluable RCC patients were treated with single agent CB-839 on the BID (twice-daily) dosing schedule. One patient achieved a partial response with a substantial decrease in target lesions (32%), including a dramatic improvement in the patient's extensive lymphadenopathy. A total of 10 patients (50%) showed stable disease or better.

We are also evaluating CB-839 in expansion cohorts in combination with everolimus and cabozantinib. In November 2016, we presented data on 15 evaluable RCC patients, including 12 clear cell patients, and three papillary patients. Ninety-three percent (93%) of these patients had disease

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control (response or stable disease); one patient had a partial response, one patient had progressive disease, and 13 patients had stable disease. The median progression free survival was 8.5 months and for the majority of patients, their time on therapy is longer than their time on treatment in their prior therapy. In the clear cell patient population the disease control rate was 100% and eight patients remain on study. Patients enrolled in the trial had advanced or metastatic disease and had received a median of two prior treatments, which included tyrosine kinase inhibitors, mTOR inhibitors, and checkpoint inhibitors. Patients were administered CB-839 in oral doses that ranged from 400-800 mg twice a day in combination with a fixed oral dose of everolimus at 10 mg once a day. The addition of CB-839 to full-dose everolimus has been well tolerated, with a similar safety profile to the known profile of everolimus alone. Grade 3 events include two events of hyperglycemia and one event each of diarrhea, anemia and fatigue. We plan to present additional data from this trial in the first quarter of 2018. In addition, we continue to enroll patients in single arm cohort of patients dosed with CB-839 in combination with cabozantinib, with data expected in 2018.

In August 2017, we initiated CX-839-005, a Phase 2 randomized, double blind, placebo controlled trial designed to evaluate the safety and efficacy of CB-839 in combination with everolimus versus placebo with everolimus in approximately 250 patients with metastatic, clear cell RCC patients who have been treated with at least two prior lines of systemic therapy including a vascular endothelial growth factor receptor-targeting tyrosine kinase inhibitor and at least one of either cabozantinib or an active PD-1/PD-L1 inhibitor. Patients will be randomized in a 2:1 ratio. The primary endpoint is progression free survival assessed by an independent review committee; overall survival will be assessed as a secondary endpoint. The multicenter, international study will be conducted at multiple sites in the United States, Europe and Canada. The U.S. Food and Drug Administration (FDA) has granted Fast Track designation to CB-839 in combination with everolimus, for the treatment of patients with metastatic RCC who have received 2 or more prior lines of therapy.

In August 2016, we initiated CX-839-004, a Phase 1/2 clinical trial of CB-839 in combination with the PD-1 inhibitor nivolumab in patients with RCC, melanoma, and non-small cell lung cancer. The Phase 1/2 study will assess the safety, pharmacokinetics and pharmacodynamics of CB-839 and nivolumab. The study will enroll patients who are either naïve to checkpoint inhibitors, had prior nivolumab therapy, or were recently treated with nivolumab without tumor response. Patients may be progressing on nivolumab or failing to respond and will receive CB-839 as an add-on therapy. In December 2016, we announced a clinical trial collaboration to evaluate Bristol-Myers Squibb's nivolumab in combination with CB-839 in two of the cohorts of patients with clear cell RCC. In May 2017, the collaboration with Bristol-Myers Squibb was expanded to include additional RCC cohorts as well as non-small cell lung cancer and melanoma (all study patients). We expect to present initial data from this trial in the fourth quarter of 2017.

Triple Negative Breast Cancer

In December 2016, we presented data on 28 TNBC patients treated with doses of CB-839 of 400, 600 or 800 mg BID in combination with 80 mg/m² IV paclitaxel, weekly, three weeks out of four; 23 were evaluable for response. The majority of patients had received at least three prior lines of therapy, with 43% of patients treated with five or more prior therapies in the advanced/metastatic setting. Most patients had received prior taxane therapy in either the neo-adjuvant or metastatic setting. Among evaluable patients treated with CB-839 doses of at least 600 mg BID (n=16), there are 5 partial responses (31%) and disease control in 11 patients (69%). In addition, the combination overcame resistance to paclitaxel in heavily pretreated TNBC patients. There was a 38% response rate and 50% disease control rate in patients who received prior taxanes in the metastatic setting. There was a 50% response rate among taxane-refractory African American patients. Four of five responding

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patients were African American. This is consistent with higher glutamine utilization observed in tumors from this population. CB-839 was well tolerated in combination with paclitaxel.

In July 2017, we initiated CX-839-007, a Phase 2 trial of CB-839 with paclitaxel in TNBC patients. Four single arm, open label, cohorts of African American and non-African American patients will be treated in both the early stage setting, where patients have no prior taxane treatment, as well as the late stage setting after prior taxane. The primary endpoint of this trial is objective response rate. We plan to present data from the TNBC development program in the fourth quarter of 2017, with additional data to be presented in 2018.

Colorectal Cancer

In 2017, an estimated 135,000 new cases of colorectal cancer (CRC) will be diagnosed in the United States according to the American Cancer Society. Researchers report that PIK3CA mutation is present in 10% to 20% of all cases of CRC. An academic research group at Case Western demonstrated that single agent CB-839 inhibits the growth of CRCs with PIK3CA mutations in immunocompromised mice, but CRC tumors with a normal PIK3CA gene were not inhibited. Remarkably, the combination of CB-839 with 5-fluorouracil induced complete and long-lasting tumor regressions in animals bearing PIK3CA mutant CRC tumors, but not tumors with normal PIK3CA, suggesting that this combinational therapy may be a unique and effective approach in the clinic. In the third quarter of 2016, an investigator-sponsored clinical trial was initiated by Drs. Jennifer Eads, Alok Khorana, and Neal Meropol at the Case Western Comprehensive Cancer Center. Enrollment in this study is ongoing.

CB-1158

Our second product candidate, CB-1158, is a first-in-class immuno-oncology metabolic checkpoint inhibitor targeting arginase, an immunosuppressive enzyme in MDSCs responsible for T-cell suppression. Significant infiltration by arginase-expressing myeloid cells has been observed in many solid tumor types including lung, colorectal esophageal, bladder, head and neck, kidney cancer, and other tumor types. We have confirmed that arginase-expressing MDSCs are found by immunohistochemistry in a wide range of tumor types including non-small cell lung (both adenocarcinoma and squamous types), gastrointestinal and bladder cancers. CB-1158 is being co-developed with Incyte.

CB-1158 entered clinical trials in September 2016, and is currently being tested in a Phase 1 clinical trial in patients with solid tumors. We presented data in June 2017 at the American Society of Clinical Oncology (ASCO) annual meeting. As of the data cut off of April 24, 2017, a total of 17 patients with advanced solid tumors had received single agent doses ranging from 50 to 150 mg twice a day (BID) in the ongoing Phase 1 trial. CB-1158 was generally well tolerated with no drug-related serious adverse events. Treatment related adverse events were limited to one case each of Grade 1 anemia, fatigue, increased ALT and myalgia. No Grade 3 treatment-related adverse events were reported. Reversible, asymptomatic elevations of urinary orotic acid, a highly sensitive marker of urea cycle inhibition, were observed in two patients at 150 mg BID. Plasma levels of arginase were inhibited > 90% in all patients, and in 10 of 11 patients plasma arginine increased 1.5-fold or more. The pharmacokinetics support BID dosing of CB-1158, as currently tested doses continuously maintained targeted levels of arginase inhibition. The trial is continuing to enroll patients in the dose escalation phase of the study, and expansion cohorts in pre-defined tumor types, to be followed by combination studies with an anti-PD-1 antibody.

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In January 2017, we entered into a global collaboration and license agreement for the research, development and commercialization of our small molecule arginase inhibitor CB-1158 in hematology and oncology with Incyte, or the Incyte Collaboration Agreement. We are collaborating with Incyte on and co-funding the development of CB-1158 for oncology and hematology indications. Incyte bears 70% and we bear 30% of global development costs, unless we opt out of development co-funding. We have the right to conduct a portion of clinical development studies under the collaboration, including combination studies of a licensed product with any other of our proprietary compounds. If we do not opt out of development co-funding, the parties will share profits and losses in the United States, with 60% to Incyte and 40% to us, and we have the right to co-detail licensed products in the United States. We retain the rights to certain arginase inhibitors for specific indications outside of hematology and oncology. In the first quarter of 2017 Incyte paid us an upfront license fee of \$45.0 million and in March 2017, we achieved a development milestone of \$12.0 million for which we received payment in May of 2017. Incyte may pay potential development, regulatory and sales milestone payments up to an additional \$418.0 million if the profit share is in effect, or an additional \$738.0 million if the profit share terminates.

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 \$133.3 million as of June 30, 2017.

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.

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

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates. If we experience delays or difficulties in enrolling patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

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

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.

Our arginase inhibitors program in hematology and oncology indications, including CB-1158, is reliant in part on Incyte for the successful development and commercialization in a timely manner. If Incyte does not devote sufficient resources to CB-1158's development, is

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unsuccessful in its efforts, or chooses to terminate its agreement with us, our business, operating results and financial condition will be harmed.

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

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be impaired.

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 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 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 until the earlier of the fifth anniversary of the closing of our initial public offering in October 2014 or until we are no longer an emerging growth company.

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 of our common stock, par value \$0.0001 per share, with an aggregate sale price of up to \$50,000,000.
Common stock to be outstanding after this offering	Up to 39,041,671 shares, assuming the sale of 3,584,229 shares of our common stock in this offering at a public offering price of \$13.95 per share, which was the last reported sale price of our common stock on the NASDAQ Global Select Market on August 17, 2017. The actual number of shares issued will vary depending on the sales price under this offering.
Manner of offering	At-the-market offering that may be made from time to time through or to Cowen, as sales agent and/or principal. See Plan of Distribution on page 18.
Use of proceeds	We intend to use the net proceeds from this offering, if any, to fund our clinical trials and for working capital and general corporate purposes. See Use of Proceeds on page 11.
Risk factors	Investment in our securities involves a high degree of risk. You should read the Risk Factors, beginning on page 8 of this prospectus and in the documents incorporated by reference into this prospectus for a discussion of factors to consider before deciding to purchase shares of our common stock.

NASDAQ Global Select Market Symbol: CALA

The number of our shares of common stock outstanding after this offering is based on 35,457,442 shares of common stock outstanding as of June 30, 2017, and excludes:

3,397,409 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2017 with a weighted-average exercise price of \$7.15 per share;

543,958 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; and

504,807 shares 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.

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RISK FACTORS

You should consider carefully the risks described below and discussed under the section titled Risk Factors contained in our Annual Report on Form 10-K for the year ended December 31, 2016, and in our subsequent Quarterly Reports on Form 10-Q as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act, each o