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/m$^2$ 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-florouracil 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**

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|---|---|
| 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 of which is incorporated by reference in this prospectus in their entirety, together with other information in this prospectus, and the information and documents incorporated by reference in this prospectus, and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our common stock. If any of the following events actually occur, our business, financial condition, results of operations or cash flow could be harmed. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. The risks below and incorporated by reference in this prospectus are not the only ones we face. Additional risks not currently known to us or that we currently deem immaterial may also affect our business operations. Please also read carefully the section below titled Special Note Regarding Forward-Looking Statements.*

### Additional Risks Relating To The Offering

***Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.***

Our management will have broad discretion over the use of proceeds from this offering. The net proceeds from this offering will be used for working capital and general corporate purposes, which may include, among other things, funding research and development, clinical trials, vendor payables, potential regulatory submissions, hiring additional personnel and capital expenditures. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses or products; however, we have no current commitments or obligations to do so.

Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or enhance the value of our common stock.

***You may experience future dilution as a result of future equity offerings.***

To raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

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## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents we have filed with the SEC that are incorporated by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

- our ability to fund our working capital requirements;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our ability to successfully commercialize our product candidates;
- the rate and degree of market acceptance of our products that are approved;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
- our expectation that our existing capital resources and the net proceeds from this offering will be sufficient to enable us to complete our planned clinical trials;
- our expectations with respect to the Incyte Collaboration Agreement;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- our ability to identify and develop new product candidates;
- our ability to retain and recruit key personnel;
- our use of proceeds from this offering;
- our financial performance; and

developments and projections relating to our competitors or our industry.

These risks are not exhaustive. Other sections of this prospectus may include additional factors that could harm our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

All statements other than statements of historical facts contained in this prospectus, including statements regarding our future financial condition, business strategy and plans, and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by words such as anticipate, believe, continue, could, design, estimate, expect, intend, may, plan, potentially, predict, sho of these terms or other similar expressions. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail many of these risks under the section titled Risk Factors contained in this prospectus, in any free writing prospectuses we may authorize for use in connection with a specific offering, and in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated

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by reference into this prospectus in their entirety. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. You should read this prospectus together with the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

In addition, statements that we believe and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

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## USE OF PROCEEDS

The amount of proceeds from this offering will depend upon the number of shares of our common stock sold and the market price at which they are sold. There can be no assurance that we will be able to sell any shares under or fully utilize the sales agreement with Cowen as a source of financing. We intend to use the net proceeds, if any, from this offering for working capital and general corporate purposes, which may include, among other things, funding research and development, clinical trials, vendor payables, potential regulatory submissions, hiring additional personnel and capital expenditures. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses or products; however, we have no current commitments or obligations to do so.

The amounts and timing of our actual expenditures will depend on numerous factors, including our development and commercialization efforts, as well as the amount of cash used in our operations. We therefore cannot estimate with certainty the amount of net proceeds to be used for the purposes described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities.

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## DILUTION

If you invest in our common stock, your interest will be diluted to the extent of the difference between the public offering price per share and the as adjusted net tangible book value per share of our common stock after this offering.

Our net tangible book value as of June 30, 2017, was $162.5 million, or $4.58 per share. Net tangible book value is total tangible assets less our total liabilities divided by the number of outstanding shares of common stock.

After giving effect to the sale of $50,000,000 of shares common stock in this offering at an assumed public offering price of $13.95 per share, which was the closing price of our common stock as reported on NASDAQ Global Select Market on August 17, 2017, and after deducting offering commissions and expenses payable by us, our net tangible book value as of June 30, 2017, would have been $210.7 million, or $5.40 per share of common stock. This represents an immediate increase in net tangible book value of $0.82 per share to our existing stockholders and an immediate dilution in net tangible book value of $8.55 per share to investors participating in this offering. The following table illustrates this dilution per share to investors participating in this offering:

| | | |
|---|---|---|
| Assumed public offering price per share | | $ 13.95 |
| Net tangible book value per share as of June 30, 2017 | $ 4.58 | |
| Increase in net tangible book value per share attributable to new investors in offering | $ 0.82 | |
| As adjusted net tangible book value per share after this offering | | 5.40 |
| Dilution per share to new investors | | $ 8.55 |

The above illustration of dilution per share to investors participating in this offering assumes no exercise of outstanding options to purchase our common stock.

The above discussion and table are based on shares of our common stock issued and outstanding after this offering as of June 30, 2017, and excludes:

- 3,397,409 shares issuable upon the exercise of options outstanding at 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 automatic increases in the number of shares of common stock reserved for future issuances under this plan; and
- 504,807 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, as well as automatic increases in the number of shares of common stock reserved for future issuances under this plan.

To the extent that any of these outstanding options are exercised, there will be further dilution to new investors.

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## DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 200,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share. The following is a summary of the rights of our common and preferred stock and some of the provisions of our amended and restated certificate of incorporation and amended and restated bylaws, an investor rights agreement between us and certain stockholders and Delaware General Corporation Law. This is only a summary, and is qualified in its entirety by reference to our certificate of incorporation, investor rights agreement and the bylaws.

### Common Stock

#### *Voting Rights*

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders. The affirmative vote of holders of at least a majority of the voting power of all of the then-outstanding shares of capital stock, voting as a single class, is required to amend certain provisions of our amended and restated certificate of incorporation, including provisions relating to amending our amended and restated bylaws, the classified board, the size of our board, removal of directors, director liability, vacancies on our board, special meetings, stockholder notices, actions by written consent and exclusive jurisdiction.

#### *Dividends*

Subject to preferences that may apply to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that our board of directors may declare out of funds legally available for that purpose on a non-cumulative basis.

#### *Liquidation*

In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding preferred stock.

#### *Rights and Preferences*

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

#### *Preferred Stock*

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the number, rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and sinking fund terms, and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control or other corporate action. We have no

current plan to issue any shares of preferred stock.

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**Stockholder Registration Rights**

Certain holders of shares of our common stock, including certain holders of five percent of our capital stock and entities affiliated with certain of our directors, are entitled to certain rights with respect to registration of such shares under the Securities Act. These shares are referred to as registrable securities. The holders of these registrable securities possess registration rights pursuant to the terms of the investor rights agreement and are described in additional detail below.

The registration of shares of our common stock pursuant to the exercise of the registration rights described below would enable the holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective. We will pay the registration expenses, other than underwriting discounts, selling commissions and stock transfer taxes, of the shares registered pursuant to the demand, piggyback and Form S-3 registrations described below.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to limit the number of shares the holders may include. The demand, piggyback and Form S-3 registration rights described below will expire three years after the effective date of the registration statement, of which this prospectus forms a part, or, with respect to any particular holder, at such time that such holder can sell its shares under Rule 144 of the Securities Act during any three-month period.

***Demand Registration Rights***

The holders of the registrable securities are entitled to certain demand registration rights. The holders of at least 60% of the registrable securities may make a written request that we register all or a portion of their shares, subject to certain specified exceptions. Such request for registration must cover securities the aggregate offering price of which, before payment of underwriting discounts and commissions, would exceed $50,000,000.

***Piggyback Registration Rights***

In connection with the filing of the registration statement of which this prospectus forms a part, the holders of registrable securities were entitled to, and the necessary percentage of holders waived, their rights to include their shares of registrable securities in the registration statement of which this prospectus forms a part. If we propose to register for offer and sale any of our securities under the Securities Act in another offering, either for our own account or for the account of other security holders, the holders of these shares will be entitled to certain piggyback registration rights allowing them to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act, including a registration statement on Form S-3 as discussed below, other than with respect to a demand registration or a registration statement on Forms S-4 or S-8 or related to stock issued upon conversion of debt securities, the holders of these shares are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their shares in the registration.

***Form S-3 Registration Rights***

The holders of the registrable securities are entitled to certain Form S-3 registration rights. Any holder of these shares can make a request that we register for offer and sale their shares on Form S-3 if we are qualified to file a registration statement on Form S-3, subject to certain specified exceptions. Such request for registration on Form S-3 must cover securities the aggregate offering price of which, before payment of the underwriting discounts and commissions, equals or exceeds $5,000,000. We will not be required to effect more than two registrations on Form S-3 within any

12 month period.

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**Anti-Takeover Provisions of Delaware Law and Our Charter Documents**

***Section 203 of the Delaware General Corporation Law***

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (1) by persons who are directors and also officers and (2) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; and
- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least $66\,^{2}/_{3}\%$ of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines a business combination to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an interested stockholder as an entity or person who, together with the person s affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status owned, 15% or more of the outstanding voting stock of the corporation.

The statute could prohibit or delay mergers or other takeover or change in control attempts and, accordingly, may discourage attempts to acquire us even though such a transaction may offer our stockholders the opportunity to sell their stock at a price above the prevailing market price.

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***Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws***

Among other things, our amended and restated certificate of incorporation and amended and restated bylaws:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate, including the right to approve an acquisition or other change of control;
- provide that the authorized number of directors may be changed only by resolution of our board of directors;
- provide that our board of directors will be classified into three classes of directors;
- provide that, subject to the rights of any series of preferred stock to elect directors, directors may only be removed for cause, which removal may be effected, subject to any limitation imposed by law, by the holders of at least a majority of the voting power of all of our then-outstanding shares of the capital stock entitled to vote generally at an election of directors;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent or electronic transmission;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder s notice;
- provide that special meetings of our stockholders may be called only by the chairman of our board of directors, our chief executive officer or by our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors; and
- not provide for cumulative voting rights, therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose.

The amendment of any of these provisions would require approval by the holders of at least 66 $^{2}/_{3}$% of the voting power of all of our then-outstanding common stock entitled to vote generally in the election of directors, voting together as a single class.

The combination of these provisions will make it more difficult for our existing stockholders to replace our board of directors as well as for another party to obtain control of us by replacing our board of directors. Since our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change our control.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to reduce our vulnerability to hostile takeovers and to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of

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delaying changes in our control or management. As a consequence, these provisions may also inhibit fluctuations in the market price of our stock that could result from actual or rumored takeover attempts. We believe that the benefits of these provisions, including increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure our company, outweigh the disadvantages of discouraging takeover proposals, because negotiation of takeover proposals could result in an improvement of their terms.

***Choice of Forum***

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. The enforceability of similar choice of forum provisions in other companies certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable.

**Listing**

Our common stock is listed on the NASDAQ Global Select Market under the symbol CALA.

**Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent s address is 6201 15th Avenue, Brooklyn, New York 11219.

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## PLAN OF DISTRIBUTION

We have entered into the sales agreement with Cowen, under which we may issue and sell from time to time up to $50,000,000 of our common stock through Cowen as our sales agent. Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an at the market offering as defined in Rule 415 under the Securities Act, including sales made directly on The NASDAQ Global Select Market or any other trading market for our common stock. If authorized by us in writing, Cowen may purchase shares of our common stock as principal.

Cowen will offer our common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. Cowen or we may suspend the offering of our common stock being made through Cowen under the sales agreement upon proper notice to the other party. Cowen and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party s sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent equals up to 3.0% of the gross sales price of the shares sold through it pursuant to the sales agreement. We have also agreed to reimburse Cowen up to $50,000 of Cowen s actual outside legal expenses incurred by Cowen in connection with this offering. We have also agreed to reimburse Cowen for its FINRA counsel fees in an amount up to $10,000. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately $300,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on The NASDAQ Global Select Market on each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the third business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of our common stock on our behalf, Cowen may be deemed to be an underwriter within the meaning of the Securities Act, and the compensation paid to Cowen may be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, Cowen will not engage in any transactions that stabilizes our common stock.

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Our common stock is listed on The NASDAQ Global Select Market and trades under the symbol CALA. The transfer agent of our common stock is American Stock Transfer & Trust Company, LLC.

Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

## LEGAL MATTERS

Cooley LLP, Palo Alto, California, will pass upon the validity of the shares of common stock offered hereby. As of the date of this prospectus, GC&H Investments, LLC and GC&H Investments, entities comprised of partners and associates of Cooley LLP, beneficially own an aggregate of 2,378 shares of our common stock. Cowen and Company, LLC is being represented by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts in connection with this offering.

## EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

## WHERE YOU CAN FIND ADDITIONAL INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC s website at http://www.sec.gov. You may also read and copy any document we file at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

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## INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-36644):

- our Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on March 16, 2017;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2017, filed with the SEC on May 9, 2017;
- our Quarterly Report on Form 10-Q for the quarter ended June 30, 2017, filed with the SEC on August 8, 2017;
- the information specifically incorporated by reference in our Annual Report on Form 10-K for the year ended December 31, 2016, from our definitive proxy statement relating to our 2017 annual meeting of stockholders, filed with the SEC on April 21, 2017;
- our Current Reports on Form 8-K filed with the SEC on January 30, 2017, March 13, 2017, March 22, 2017, May 15, 2017 and June 14, 2017; and
- the description of our common stock in our registration statement on Form 8-A filed with the SEC on September 25, 2014.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, until we file a post-effective amendment that indicates the termination of the offering of the shares of our common stock made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Calithera Biosciences, Inc.

343 Oyster Point Blvd. Suite 200

South San Francisco, California 94080

(650) 870-1000

Attn: Secretary

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**$50,000,000**

**Common Stock**

**PROSPECTUS**

**Cowen**

**August 18, 2017**