

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

Form 424B5

November 12, 2013

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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-180533

Prospectus Supplement

(To prospectus dated May 1, 2012)

Up to \$30,000,000 of Shares

Common Stock

We have entered into an amendment to a sales agreement with Cantor Fitzgerald & Co. relating to shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the amended sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$30,000,000 from time to time through Cantor Fitzgerald & Co., acting as agent.

Our common stock is listed on The NASDAQ Global Select Market under the symbol PACB. On November 7, 2013, the last reported sale price of our common stock on The NASDAQ Global Select Market was \$3.92 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made in sales deemed to be at-the-market equity offerings as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through The NASDAQ Global Select Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law. Cantor Fitzgerald & Co. will act as sales agent on a best effort basis and use commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms between Cantor Fitzgerald & Co. and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Cantor Fitzgerald & Co. will be entitled to compensation at a fixed commission rate of 3.0% of the gross sales price per share sold. In connection with the sale of the common stock on our behalf, Cantor Fitzgerald & Co. will be deemed to be an underwriter within the meaning of the Securities Act, and the compensation of Cantor Fitzgerald & Co. will be deemed to be underwriting commissions or discounts.

Investing in our securities involves a high degree of risk. Before making an investment decision, please read the information contained in or incorporated by reference under the heading Risk Factors beginning on page S-4 of this prospectus supplement, on page 3 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.

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

The date of this prospectus supplement is November 12, 2013.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus relate to the offering of our common stock. Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus supplement, the accompanying prospectus, any free writing prospectus that we have authorized for use in connection with this offering, and the information incorporated by reference as described under the headings

Where You Can Find More Information and Incorporation of Certain Information by Reference in this prospectus supplement. These documents contain important information that you should consider when making your investment decision.

This document is comprised of two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also adds to, and updates information contained in, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus, including the documents incorporated by reference into the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to the combined document consisting of this prospectus supplement and the accompanying prospectus. In this prospectus supplement, as permitted by law, we incorporate by reference information from other documents that we file with the Securities and Exchange Commission, or the Commission. This means that we can disclose important information to you by referring to those documents. The information incorporated by reference is considered to be a part of this prospectus supplement and the accompanying prospectus and should be read with the same care. When we update the information contained in documents that have been incorporated by reference by making future filings with the Commission, the information included or incorporated by reference in this prospectus supplement is considered to be automatically updated and superseded. In other words, in case of a conflict or inconsistency between information contained in this prospectus supplement and information in the accompanying prospectus or incorporated by reference into this prospectus supplement, you should rely on the information contained in the document that was filed later.

You should rely only on the information contained in, or incorporated by reference into, this prospectus supplement, the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering. We have not authorized any other person to provide you with different information. We are not making an offer to sell or soliciting an offer to buy our securities in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations, and prospects may have changed since those dates.

Unless the context otherwise requires, as used in this prospectus supplement, we, us, Pacific Biosciences, PacBio, the Company and our Pacific Biosciences of California, Inc., a Delaware corporation.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement or the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our securities. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information and financial statements and related notes thereto in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference into this prospectus supplement and the accompanying prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information referred to under the heading "Risk Factors" in this prospectus supplement on page S-4, in the accompanying prospectus on page 3 and in the documents incorporated by reference into this prospectus supplement.

Overview

We develop, manufacture and market an integrated platform for high resolution genetic analysis. We have developed a technology to study the synthesis, composition, structure and regulation of DNA. Combining advances in nanofabrication, biochemistry, molecular biology, surface chemistry and optics, we created a technology platform called single molecule, real-time, or SMRT, technology. Our SMRT technology uses the natural processing power of enzymes, combined with specially designed reagents and detection systems, to record individual biochemical events as they occur. The ability to observe single molecule events in real time provides the scientific community with an advanced tool for investigating basic biochemical processes such as DNA synthesis. Our SMRT technology has the potential to advance scientific understanding by providing a window into biological processes that has not previously been open.

Our initial focus is to offer our SMRT technology to the DNA sequencing market where we have developed and introduced a third generation sequencing platform, the PacBio RS High Resolution Genetic Analyzer and the PacBio RS II Sequencing System. The PacBio RS and the PacBio RS II maintain many of the key attributes of first and second generation sequencing technologies while solving many of their inherent limitations, including short readlengths, limited flexibility, long time to result, complex sample preparation and risk of amplification bias. Our system provides long readlengths, flexibility in experimental design, fast time to result, and ease of use. The PacBio RS and the PacBio RS II each consist of an instrument platform that uses the Company's proprietary consumables, including its SMRT Cells and several chemical reagent kits used to prepare and sequence DNA samples. Our system is designed to be integrated into existing laboratory workflows and information systems.

Company Information

Pacific Biosciences was incorporated in the State of Delaware in 2000. Our executive offices are located at 1380 Willow Road, Menlo Park, California 94025, and our telephone number is (650) 521-8000. We maintain a website at www.pacificbiosciences.com where general information about us is available. Our website, and the information contained therein, is not a part of this prospectus supplement.

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THE OFFERING

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| Common stock offered by us | Shares of our common stock having an aggregate offering price of up to \$30 million. |
| Common stock to be outstanding after this offering | Up to 73,796,185 shares, assuming sales at a price of \$3.92 per share, which was the closing price on The NASDAQ Global Select Market on November 7, 2013. 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 our sales agent, Cantor Fitzgerald & Co. See Plan of Distribution on page S-8. |
| Use of proceeds | We currently intend to use the net proceeds from this offering, if any, for general corporate purposes, including capital expenditures and working capital. We may also use a portion of the net proceeds from this offering to acquire or invest in complementary businesses, technologies, product candidates or other intellectual property. See Use of Proceeds on page S-7 of this prospectus supplement. |
| Risk factors | Investing in our securities involves a high degree of risk. Before making an investment decision, you should read the information contained in or incorporated by reference under the heading Risk Factors beginning on page S-4 of this prospectus supplement, on page 3 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement. |

Nasdaq Global Select Market symbol

PACB

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 66,143,124 shares outstanding as of September 30, 2013. The number of shares outstanding as of September 30, 2013, as used throughout this prospectus supplement, unless otherwise indicated, excludes the following, all as of September 30, 2013:

11,610,550 shares of our common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price of \$5.18 per share;

4,762,611 shares of common stock reserved for future issuance under our 2010 Equity Incentive Plan, 2010 Outside Director Equity Incentive Plan and our 2010 Employee Stock Purchase Plans; and

outstanding warrants to purchase an aggregate of 5,503,722 shares of common stock at a weighted average exercise price of \$2.63 per share.

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RISK FACTORS

An investment in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described below and discussed under the section entitled "Risk Factors" contained in our Annual Report on Form 10-K for the year ended December 31, 2012, and any subsequent Quarterly Report on Form 10-Q, which are incorporated by reference into this prospectus supplement and the accompanying prospectus in its entirety, together with other information in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering. The risks described in these documents are not the only ones we face, but those that we currently consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below entitled "Forward-Looking Statements."

Additional Risks Related to This Offering and our Securities

Management will have broad discretion as to the use of the proceeds from this offering and may not use the proceeds effectively.

Because we have not designated the amount of net proceeds from this offering to be used for any particular purpose, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of the offering. Our management may use the net proceeds for corporate purposes that may not improve our financial condition or market value.

You may experience dilution.

Given effect to the issuance of common stock in this offering, the receipt of the expected net proceeds and the use of those proceeds, this offering may have a dilutive effect on our expected net income available to our common stockholders per share and funds from operations per share. The actual amount of dilution cannot be determined at this time and will be based on a number of factors. In addition, we are not restricted from issuing additional securities in the future, including shares of common stock, securities that are convertible into or exchangeable for, or that represent the right to receive, common stock or substantially similar securities. The issuance of these securities may cause further dilution to our stockholders.

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

To the extent that we raise additional funds through the sale of equity or convertible debt securities, the issuance of such securities will result in dilution to our stockholders. 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.

The price of our common stock has been and may continue to be highly volatile, which may make it difficult for stockholders to sell our common stock when desired or at attractive prices.

The market price of our common stock is highly volatile, and we expect it to continue to be volatile for the foreseeable future. For example, from November 8, 2012 through November 7, 2013, our common stock traded at a low price of \$1.06 and a high price of \$6.50. Some of the factors that may cause the market price of our common stock to continue to fluctuate include:

actual or anticipated fluctuations in our bookings, financial condition and operating results;

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announcements of technological innovations by us or our competitors;

overall conditions in our industry and market;

addition or loss of significant customers;

changes in laws or regulations applicable to our products;

actual or anticipated changes in our growth rate relative to our competitors;

announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;

additions or departures of key personnel;

competition from existing products or new products that may emerge;

issuance of new or updated research or reports by securities analysts;

fluctuations in the valuation of companies perceived by investors to be comparable to us;

disputes or other developments related to proprietary rights, including patents, litigation matters and our ability to obtain intellectual property protection for our technologies;

announcement or expectation of additional financing efforts;

sales of our common stock by us or our stockholders;

share price and volume fluctuations attributable to inconsistent trading volume levels of our shares; and

general economic and market conditions.

The stock market in general, and The NASDAQ Global Select Market and the market for companies in our industry in particular, have experienced extreme price and volume fluctuations that may have been unrelated or disproportionate to the operating performance of the listed companies. There have been dramatic fluctuations in the market prices of securities of biotechnology companies. These price fluctuations may be rapid and severe and may leave investors little time to react. Broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. Sharp drops in the market price of our common stock may also expose us to securities class-action litigation.

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public markets could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We have agreed, without the prior written consent of Cantor Fitzgerald & Co. and subject to certain exceptions set forth in the sales agreement, not to sell or otherwise dispose of any common stock or securities convertible into or exchangeable for shares of common stock, warrants or any rights to purchase or acquire common stock during the period beginning on the fifth trading day immediately prior to the delivery of any placement notice delivered by us to Cantor Fitzgerald & Co. and ending on the fifth trading day immediately following the final settlement date with respect to the shares sold pursuant to such notice. We have further agreed, subject to certain exceptions set forth in the sales agreement, not to sell or otherwise dispose of any common stock or securities convertible into or exchangeable for shares of common stock, warrants or any rights to purchase or acquire common stock in any other at-the-market or continuous equity transaction prior to the termination of the sales agreement with Cantor Fitzgerald & Co. We cannot predict the effect that future sales of our common stock would have on the market price of our common stock.

We do not anticipate paying dividends on our capital stock.

We do not intend to pay dividends on our capital stock in the foreseeable future. The declaration of dividends is subject to the discretion of our Board of Directors and will depend on various factors, including our

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operating results, financial condition, future prospects and any other factors deemed relevant by our board of directors. You should not rely on an investment in our company if you require dividend income from your investment in our company. The success of your investment will likely depend entirely upon any future appreciation of the market price of our capital stock, which is uncertain and unpredictable. There is no guarantee that our capital stock will appreciate in value or even maintain the price at which you purchased your shares.

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FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents we have filed with the Commission that are incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve risks and uncertainties, as well as assumptions, that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Forward-looking statements generally are identified by the words may, will, project, might, expects, anticipates, believes, intends, estimates, should, could, would, strategy, plan, or other words or expressions of similar meaning. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. For example, forward-looking statements include statements about our future financial and operating results, plans, expectations for potential research and development payments, milestone payments, royalty payments, cash burn rates, timing of achieving positive cash flow, potential revenue and profits of a combined company or from license agreements, costs and expenses, interest rates, outcome of contingencies, financial condition, liquidity, business strategies and cost savings, any statements of the plans, strategies and objectives of management for future operations, any statements concerning our product candidates and product development, any statements regarding future economic conditions or performance, statements of belief and any statement of assumptions underlying any of the foregoing. We discuss in greater detail, and incorporate by reference into this prospectus supplement and the accompanying prospectus in their entirety, many of these risks and uncertainties under the heading Risk Factors beginning on page S-4 of this prospectus supplement. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements.

If any of these risks or uncertainties materializes or any of these assumptions proves incorrect, our results could differ materially from the expectations in these statements.

The forward-looking statements included in this prospectus supplement are made only as of the date of this prospectus supplement, and we are not under any obligation to update our respective forward-looking statements and do not intend to do so. You should not assume that the information contained in this prospectus supplement or the accompanying prospectus is accurate as of any date other than the date on the front of this prospectus supplement or the accompanying prospectus, as applicable, or that any information incorporated by reference into this prospectus supplement or the accompanying prospectus is accurate as of any date other than the date of the document so incorporated by reference.

You should read this prospectus supplement, the accompanying prospectus, the documents we have filed with the Commission that are incorporated by reference and any free writing prospectus that we have authorized 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.

USE OF PROCEEDS

We currently intend to use the net proceeds from this offering, if any, for general corporate purposes, including capital expenditures and working capital. We may also use a portion of the net proceeds from this offering to acquire or invest in complementary businesses, technologies, product candidates or other intellectual property, although we have no present commitments or agreements to do so.

As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. As a result, our management will have broad discretion regarding the timing and application of the net proceeds from this offering. Pending the uses described above, we intend to invest the net proceeds in interest-bearing, investment-grade securities.

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PLAN OF DISTRIBUTION

On October 5, 2012, we entered into a Controlled Equity Offering Sales Agreement, or the sales agreement, with Cantor Fitzgerald & Co., or Cantor, under which we may issue and sell shares of our common stock having an aggregate offering price of up to \$30,000,000 from time to time through Cantor acting as agent. We have entered into an amendment to the sales agreement, or the sales agreement amendment, on November 8, 2013, primarily to provide for up to an additional \$30.0 million in aggregate offering price of shares of our common stock under the sales agreement. In addition, we currently have common stock remaining available for sale pursuant to the sales agreement and the prospectus supplement dated October 5, 2012. The sales agreement was filed as an exhibit to our Current Report on Form 8-K filed with the Securities and Exchange Commission on October 5, 2012 and is incorporated by reference in this prospectus supplement. The sales agreement amendment will be filed as an exhibit to a Current Report on Form 8-K and will be incorporated by reference in this prospectus supplement. See [Where You Can Find More Information](#) and [Incorporation of Certain Information by Reference](#) below.

Cantor may sell our common stock by any method permitted by law that is deemed to be an at-the-market offering as defined in Rule 415 promulgated under the Securities Act, including sales made directly on or through The NASDAQ Global Select Market or any other existing trading market for our common stock or to or through a market maker. Cantor may also sell our common stock by any other method permitted by law, including in privately negotiated transactions. We may instruct Cantor not to sell common stock if the sales cannot be effected at or above the price designated by us from time to time. We or Cantor may suspend the offering of our common stock upon notice and subject to other conditions.

We will pay Cantor a commission, in cash, for its services in acting as agent in the sale of our common stock. Cantor will be entitled to compensation at a fixed commission rate of 3.0% of the gross sales price per share sold. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We estimate that the total expenses for the offering, excluding compensation payable to Cantor under the terms of the sales agreement, as amended, will be approximately \$54,000.

Settlement for sales of common stock will occur on the third trading day following the date on which any sales are made, or on some other date that is agreed upon by us and Cantor in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Cantor may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Cantor will use its commercially reasonable efforts, consistent with its sales and trading practices to solicit offers to purchase the shares of our common stock under the terms and subject to the conditions set forth in the sales agreement, as amended. In connection with the sale of the common stock on our behalf, Cantor will be deemed to be an underwriter within the meaning of the Securities Act, and the compensation of Cantor will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Cantor against certain civil liabilities, including liabilities under the Securities Act. The offering of our common stock pursuant to the sales agreement, as amended, will terminate upon the earlier of (i) the sale of all shares of our common stock subject to the sales agreement, as amended, or (ii) termination of the sales agreement, as amended, as permitted therein. We and Cantor may each terminate the sales agreement, as amended, at any time upon ten days prior notice.

Cantor and its affiliates may in the future provide various investment banking, commercial banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M under the Exchange Act, Cantor will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement.

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This prospectus supplement and the accompanying prospectus in electronic format may be made available on a website maintained by Cantor, and Cantor may distribute the prospectus supplement and the accompanying prospectus electronically.

LEGAL MATTERS

The validity of the securities offered by this prospectus supplement will be passed upon by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Cantor is being represented in connection with this offering by Reed Smith LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2012, and the effectiveness of our internal control over financial reporting as of December 31, 2012, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements and our management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2012 are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

The consolidated financial statements incorporated in this prospectus supplement and the registration statement by reference to the Annual Report on Form 10-K for the year ended December 31, 2012 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 we filed with the Commission under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying 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 supplement and the accompanying 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 Commission. Our filings with the Commission are available to the public over the Internet at the Commission's website at <http://www.sec.gov>. You may also read and copy any document we file at the Commission's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the Commission at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The Commission allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus supplement. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and information contained in this prospectus supplement and the accompanying prospectus and later information that we file with the Commission will automatically update and supersede prior information. We incorporate by reference the documents listed below and any future filings (other than Current Reports on Form 8-K furnished under Item 2.02 or Item 7.01 and exhibits filed on such form that are related to such items) we make with the Commission under Sections 13(a),

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13(c), 14 or 15(d) of the Exchange Act after the date of the prospectus supplement and before the sale of all the securities covered by this prospectus supplement:

our Annual Report on Form 10-K for the year ended December 31, 2012, including the information specifically incorporated by reference into the Form 10-K from our definitive proxy statement for our 2013 Annual Meeting of Stockholders;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2013, June 30, 2013 and September 30, 2013;

our Current Reports on Form 8-K filed on October 5, 2012, February 5, 2013, March 7, 2013, May 22, 2013, July 18, 2013 and September 25, 2013 (in each case, not including any information furnished under Items 2.02 or 7.01 of Form 8-K, including the related exhibits, which information is not incorporated by reference herein); and

the description of our common stock contained in our Registration Statement on Form 8-A filed on October 6, 2010, and any amendment or report filed for the purposes of updating such description.

To the extent that any information contained in any filings we have made or will make with the Commission under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, or any exhibit thereto, was furnished, rather than filed with the Commission, such information or exhibit is specifically not incorporated by reference in this prospectus supplement.

These documents may also be accessed on our website at www.pacificbiosciences.com. Except as otherwise specifically incorporated by reference in this prospectus supplement, information contained in, or accessible through, our website is not a part of this prospectus supplement.

We will furnish without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents by writing or telephoning us at the following address:

Pacific Biosciences of California, Inc.

1380 Willow Road

Menlo Park, CA 94025

Attn: Investor Relations

(650) 521-8000

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PROSPECTUS

\$150,000,000

Pacific Biosciences of California, Inc.

By this prospectus, Pacific Biosciences may offer, from time to time:

Common stock
Preferred stock
Depositary Shares
Warrants
Debt securities
Units

Pacific Biosciences of California, Inc. a Delaware corporation (Pacific Biosciences or PacBio) may offer and sell from time to time, in one or more series or issuances and on terms that Pacific Biosciences will determine at the time of the offering, any combination of the securities described in this prospectus, up to an aggregate amount of \$150,000,000.

We will provide specific terms of any offering in a supplement to this prospectus. Any prospectus supplement may also add, update, or change information contained in this prospectus. You should carefully read this prospectus and the applicable prospectus supplement as well as the documents incorporated or deemed to be incorporated by reference in this prospectus before you purchase any of the securities offered hereby.

These securities may be offered and sold in the same offering or in separate offerings; to or through underwriters, dealers, and agents; or directly to purchasers. The names of any underwriters, dealers, or agents involved in the sale of our securities, their compensation and any over-allotment options held by them will be described in the applicable prospectus supplement. For a more complete description of the plan of distribution of these securities, see the section entitled Plan of Distribution beginning on page 25 of this prospectus.

Our common stock is listed on the Nasdaq Global Select Market under the symbol PACB. We will provide information in any applicable prospectus supplement regarding any listing of securities other than shares of our common stock on any securities exchange.

INVESTING IN OUR SECURITIES INVOLVES SIGNIFICANT RISKS. SEE RISK FACTORS BEGINNING ON PAGE 3 OF THIS PROSPECTUS AND IN THE APPLICABLE PROSPECTUS SUPPLEMENT BEFORE INVESTING IN ANY SECURITIES.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ADEQUACY OR ACCURACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is May 1, 2012

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the United States Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this shelf process, we may, from time to time, sell any combination of the securities described in this prospectus in one or more offerings up to a total amount of \$150,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add to, update or change information contained in the prospectus and, accordingly, to the extent inconsistent, information in this prospectus is superseded by the information in the prospectus supplement.

The prospectus supplement to be attached to the front of this prospectus may describe, as applicable: the terms of the securities offered; the initial public offering price; the price paid for the securities; net proceeds; and the other specific terms related to the offering of the securities.

You should only rely on the information contained or incorporated by reference in this prospectus and any prospectus supplement or issuer free writing prospectus relating to a particular offering. No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in this prospectus, any accompanying prospectus supplement and any related issuer free writing prospectus in connection with the offering described herein and therein, and, if given or made, such information or representations must not be relied upon as having been authorized by us. Neither this prospectus nor any prospectus supplement nor any related issuer free writing prospectus shall constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits.

You should read the entire prospectus and any prospectus supplement and any related issuer free writing prospectus, as well as the documents incorporated by reference into this prospectus or any prospectus supplement or any related issuer free writing prospectus, before making an investment decision. Neither the delivery of this prospectus or any prospectus supplement or any issuer free writing prospectus nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference herein or in any prospectus supplement or issuer free writing prospectus is correct as of any date subsequent to the date hereof or of such prospectus supplement or issuer free writing prospectus, as applicable. You should assume that the information appearing in this prospectus, any prospectus supplement or any document incorporated by reference is accurate only as of the date of the applicable documents, regardless of the time of delivery of this prospectus or any sale of securities. Our business, financial condition, results of operations and prospects may have changed since that date.

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Prospectus Summary

This summary description about us and our business highlights selected information contained elsewhere in this prospectus or incorporated in this prospectus by reference. This summary does not contain all of the information you should consider before buying securities in this offering. You should carefully read this entire prospectus and any applicable prospectus supplement, including each of the documents incorporated herein or therein by reference, before making an investment decision. As used in this prospectus, we, us, Pacific Biosciences, PacBio, the Company and our refer to Pacific Biosciences of California, Inc., a Delaware corporation.

Pacific Biosciences of California, Inc.

Overview

Pacific Biosciences develops, manufactures and markets an integrated platform for genetic analysis. The Company has developed a technology to study the synthesis and regulation of DNA. Combining recent advances in nanofabrication, biochemistry, molecular biology, surface chemistry and optics, Pacific Biosciences created a technology platform using its proprietary single molecule, real-time, or SMRT, technology. Pacific Biosciences' SMRT technology uses the natural processing power of enzymes, combined with specially designed reagents and detection systems, to record individual biochemical events as they occur. The ability to observe single molecule events in real time provides the scientific community with an advanced tool for investigating basic biochemical processes such as DNA synthesis. Pacific Biosciences' SMRT technology has the potential to advance scientific understanding by providing a window into biological processes that has not previously been open.

Pacific Biosciences' initial focus is on the DNA sequencing market where it has developed and introduced a third generation sequencing platform using its proprietary SMRT technology, the PacBio RS. The PacBio RS maintains many of the key attributes of first and second generation sequencing technologies while solving many of their inherent limitations, including short readlengths, limited flexibility, long time to result, complex sample preparation and risk of amplification bias. Pacific Biosciences' system provides long readlengths, flexibility in experimental design, fast time to result, and ease of use. The PacBio RS consists of an instrument platform that uses the Company's proprietary consumables, which are currently comprised of SMRT Cells and several chemical reagent kits used to prepare and sequence DNA samples. Pacific Biosciences' system is designed to be integrated into existing laboratory workflows and information systems. The Company began commercial shipments of PacBio RS instruments in April 2011.

Corporate Information

Pacific Biosciences was incorporated in the State of Delaware in 2000. Its executive offices are located at 1380 Willow Road, Menlo Park, California 94025, and its telephone number is (650) 521-8000. The Company maintains a website at www.pacificbiosciences.com where general information about us is available. The Company's website, and the information contained therein, is not a part of this prospectus.

The Securities We May Offer

We may offer up to \$150,000,000 of common stock, preferred stock, depositary shares, warrants, debt securities and/or units in one or more offerings and in any combination. This prospectus provides you with a general description of the securities we may offer. A prospectus supplement, which we will provide each time we offer securities, will describe the specific amounts, prices and terms of the securities we determine to offer.

Common Stock

We may offer shares of our common stock, par value \$0.001 per share, either alone or underlying other registered securities convertible or exercisable into our common stock. Each holder of our common stock is

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entitled to one vote for each share on all matters to be voted upon by the stockholders. Holders of our common stock are entitled to receive ratably the dividends, if any, as may be declared from time to time by our board of directors out of funds legally available therefor. If there is a liquidation, dissolution or winding up of our company, holders of our common stock would be entitled to share in our assets remaining after the payment of liabilities and any preferential rights of any outstanding preferred stock. The holders of common stock have no preemptive rights. Currently, we do not pay a dividend and do not anticipate paying cash dividends in the foreseeable future.

Preferred Stock and Depositary Shares

Under the terms of our amended and restated certificate of incorporation, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

We may also issue fractional shares of preferred stock that will be represented by depositary shares and depositary receipts.

Each series of preferred stock, depositary shares or depositary receipts, if issued, will be more fully described in the particular prospectus supplement that will accompany this prospectus, including redemption provisions, rights in the event of our liquidation, dissolution or winding up, voting rights and rights to convert into common stock. We do not have any shares of our preferred stock, depositary shares or depositary receipts presently outstanding.

Warrants

We may issue warrants for the purchase of common stock, preferred stock or debt securities. We may issue warrants independently or together with other securities.

Debt Securities

We may offer secured or unsecured obligations in the form of one or more series of senior or subordinated debt. The senior debt securities and the subordinated debt securities are together referred to in this prospectus as the debt securities. The subordinated debt securities generally will be entitled to payment only after payment of our senior debt. Senior debt generally includes all debt for money borrowed by us, except debt that is stated in the instrument governing the terms of that debt to be not senior to, or to have the same rank in right of payment as, or to be expressly junior to, the subordinated debt securities. We may issue debt securities that are convertible into shares of our common stock.

The senior and subordinated debt securities will be issued under separate indentures between us and a trustee. We have summarized the general features of the debt securities to be governed by the indentures. These indentures have been filed as exhibits to the registration statement of which this prospectus forms a part. We encourage you to read these indentures. Instructions on how you can get copies of these documents are provided under the heading *Where You Can Find More Information*.

Units

We may issue units comprised of one or more of the other classes of securities issued by us as described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit.

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RISK FACTORS

An investment in our securities involves a high degree of risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under Item 1A, "Risk Factors," in our Annual Report on Form 10-K for the fiscal year ended December 31, 2011 and any updates described in our Quarterly Reports on Form 10-Q, all of which are incorporated herein by reference, and may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future and any prospectus supplement related to a particular offering. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. The occurrence of any of these known or unknown risks might cause you to lose all or part of your investment in the offered securities.

FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain certain statements that constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. The words "anticipate," "expect," "believe," "goal," "plan," "intend," "estimate," "may," "will," "expressions and variations thereof are intended to identify forward-looking statements, but are not the exclusive means of identifying such statements. Those statements appear in this prospectus, any accompanying prospectus supplement and the documents incorporated herein and therein by reference, particularly in the sections entitled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business," and include statements regarding the intent, belief or current expectations of the company and management that are subject to known and unknown risks, uncertainties and assumptions and other factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to those discussed in the section titled "Risk Factors" set forth above.

This prospectus, any prospectus supplement and the information incorporated by reference in this prospectus and any prospectus supplement also contain statements that are based on management's current expectations and beliefs, including estimates and projections about our company, industry, financial condition, results of operations and other matters. These statements are not guarantees of future performance and are subject to numerous risks, uncertainties, and assumptions that are difficult to predict.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely upon forward-looking statements as predictions of future events. The events and circumstances reflected in the forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, including the securities laws of the United States and the rules and regulations of the SEC, we do not plan to publicly update or revise any forward-looking statements contained herein after we distribute this prospectus, whether as a result of any new information, future events or otherwise.

Table of Contents**RATIO OF EARNINGS TO FIXED CHARGES**

Our earnings are inadequate to cover fixed charges. The following table sets forth the dollar amount of the coverage deficiency for each of the years ended December 31, 2011, 2010, 2009, 2008 and 2007. We have not included a ratio of earnings to combined fixed charges and preferred stock dividends because we do not have any earnings. We have derived the deficiency of earnings to cover fixed charges from our historical financial statements. The following should be read in conjunction with our consolidated financial statements, including the notes thereto, and the other financial information included or incorporated by reference herein. See Exhibit 12.1 hereto for additional detail regarding the computation of the deficiency of earnings to cover fixed charges.

| | Fiscal Year Ended December 31, | | | | |
|---|--------------------------------|--------------|-------------|-------------|-------------|
| | 2011 | 2010 | 2009 | 2008 | 2007 |
| <i>(dollars in thousands)</i> | | | | | |
| Deficiency of earnings available to cover fixed charges (1) | \$ (109,388) | \$ (140,166) | \$ (87,703) | \$ (43,754) | \$ (21,518) |

(1) Because of the deficiency of earnings available to cover fixed charges, the ratio information is not applicable.

USE OF PROCEEDS

Unless otherwise indicated in the prospectus supplement, we will use the net proceeds from the sale of securities offered by this prospectus for general corporate purposes, which may include working capital, capital expenditures, other corporate expenses and acquisitions of complementary products, technologies or businesses. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business. As a result, unless otherwise indicated in the prospectus supplement, our management will have broad discretion to allocate the net proceeds of the offerings. Pending their ultimate use, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing instruments.

DESCRIPTION OF CAPITAL STOCK

The following information describes our common stock and preferred stock, as well as certain provisions of our amended and restated certificate of incorporation and bylaws. This description is only a summary. You should also refer to our certificate of incorporation and bylaws, which have been filed with the SEC as exhibits to our registration statement, of which this prospectus forms a part.

General

Our authorized capital stock consists of 1,000,000,000 shares of common stock with a \$0.001 par value per share, and 50,000,000 shares of undesignated preferred stock with a \$0.001 par value per share. Our board of directors may establish the rights and preferences of the preferred stock from time to time. As of February 17, 2012, there were 55,064,117 shares of common stock issued and outstanding.

The following is a summary of the material provisions of the common stock and preferred stock provided for in our amended and restated certificate of incorporation and bylaws. For additional detail about our capital stock, please refer to our certificate of incorporation and bylaws, each as amended.

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Common Stock

Each holder of our common stock is entitled to one vote for each share on all matters to be voted upon by the stockholders. Subject to any preferential rights of any outstanding preferred stock, holders of our common stock are entitled to receive ratably the dividends, if any, as may be declared from time to time by the board of directors out of funds legally available therefor. We have never declared or paid any cash dividend on our capital stock and do not anticipate paying any cash dividends in the foreseeable future. In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in our assets remaining after the payment of liabilities and any preferential rights of any outstanding preferred stock.

Holders of our common stock have no preemptive or conversion rights or other subscription rights, and there are no redemption or sinking fund provisions applicable to the common stock. The outstanding shares of common stock are fully paid and non-assessable. 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 preferred stock that we may designate and issue in the future.

Our common stock is listed on the NASDAQ Global Select Market under the symbol PACB. The transfer agent and registrar for the common stock is Computershare Shareowner Services LLC. Its address is 480 Washington Boulevard, Jersey City, NJ 07310, and its telephone number is 1-866-401-4874.

Preferred Stock

The following description of preferred stock and the description of the terms of any particular series of preferred stock that we choose to issue hereunder and that will be set forth in the related prospectus supplement are not complete. These descriptions are qualified in their entirety by reference to our amended and restated certificate of incorporation and the certificate of designation relating to any series of preferred stock. The rights, preferences, privileges and restrictions of the preferred stock of each series will be fixed by the certificate of designation relating to that series. The prospectus supplement also will contain a description of certain United States federal income tax consequences relating to the purchase and ownership of the series of preferred stock that is described in the prospectus supplement.

Under the terms of our amended and restated certificate of incorporation, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. There are no restrictions presently on the repurchase or redemption of any shares of our preferred stock.

The prospectus supplement for a series of preferred stock will specify:

the maximum number of shares;

the designation of the shares;

the annual dividend rate, if any, whether the dividend rate is fixed or variable, the date or dates on which dividends will accrue, the dividend payment dates, and whether dividends will be cumulative;

the price and the terms and conditions for redemption, if any, including redemption at our option or at the option of the holders, including the time period for redemption, and any accumulated dividends or premiums;

the liquidation preference, if any, and any accumulated dividends upon the liquidation, dissolution or winding up of our affairs;

any sinking fund or similar provision, and, if so, the terms and provisions relating to the purpose and operation of the fund;

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the terms and conditions, if any, for conversion or exchange of shares of any other class or classes of our capital stock or any series of any other class or classes, or of any other series of the same class, or any other securities or assets, including the price or the rate of conversion or exchange and the method, if any, of adjustment;

the voting rights; and

any or all other preferences and relative, participating, optional or other special rights, privileges or qualifications, limitations or restrictions.

The issuance of shares of preferred stock will affect, and may adversely affect, the rights of holders of common stock. It is not possible to state the actual effect of the issuance of any shares of preferred stock on the rights of holders of common stock until our board of directors determines the specific rights attached to that preferred stock. The effects of issuing additional preferred stock could include one or more of the following:

restricting dividends on the common stock;

diluting the voting power of the common stock;

impairing the liquidation rights of the common stock; or

delaying or preventing changes in control or management of our company.

Preferred stock will be fully paid and nonassessable upon issuance.

Effect of Certain Provisions of our Amended and Restated Certificate of Incorporation and Bylaws and the Delaware Anti-Takeover Statute

Some provisions of Delaware law and our amended and restated certificate of incorporation and bylaws contain provisions that could make the following transactions more difficult:

acquisition of us by means of a tender offer;

acquisition of us by means of a proxy contest or otherwise; or

removal of our incumbent officers and directors.

Those provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids and to promote stability in our management. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

Amended and Restated Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and our bylaws provide for the following:

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Undesignated Preferred Stock. The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue one or more series of preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of our company. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings. Our bylaws provide that in general a special meeting of stockholders may be called only by our board of directors, its chairman or our president.

Requirements for Advance Notification of Stockholder Nominations and Proposals. Our bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of our board of directors or a committee of the board of directors.

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Board Classification. Our board of directors is divided into three classes. The directors in each class are elected to serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Limits on Ability of Stockholders to Act by Written Consent. We have provided in our bylaws that our stockholders may not act by written consent. This limit on the ability of our stockholders to act by written consent may lengthen the amount of time required to take stockholder actions. As a result, a holder controlling a majority of our capital stock would not be able to amend our bylaws or remove directors without holding a meeting of our stockholders called in accordance with our bylaws.

Amendment of Certificate of Incorporation and Bylaws. The amendment of the above provisions of our amended and restated certificate of incorporation and bylaws requires approval by holders of at least two-thirds of our outstanding capital stock entitled to vote generally in the election of directors.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging, under certain circumstances, in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder unless:

prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which 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 commenced, excluding for purposes of determining the voting stock outstanding, but not for determining the outstanding voting stock owned by the interested stockholder, (i) shares owned by persons who are directors and also officers, and (ii) shares owned by 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; or

at or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66-2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock.

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DESCRIPTION OF THE DEPOSITARY SHARES

General

At our option, we may elect to offer fractional shares of preferred stock, rather than full shares of preferred stock. If we do elect to offer fractional shares of preferred stock, we will issue receipts for depositary shares and each of these depositary shares will represent a fraction of a share of a particular series of preferred stock, as specified in the applicable prospectus supplement. Each owner of a depositary share will be entitled, in proportion to the applicable fractional interest in shares of preferred stock underlying that depositary share, to all rights and preferences of the preferred stock underlying that depositary share. These rights may include dividend, voting, redemption and liquidation rights.

The shares of preferred stock underlying the depositary shares will be deposited with a bank or trust company selected by us to act as depositary, under a deposit agreement by and among us, the depositary and the holders of the depositary receipts. The depositary will be the transfer agent, registrar and dividend disbursing agent for the depositary shares.

The depositary shares will be evidenced by depositary receipts issued pursuant to the depositary agreement. Holders of depositary receipts agree to be bound by the deposit agreement, which requires holders to take certain actions such as filing proof of residence and paying certain charges.

The summary of terms of the depositary shares contained in this prospectus is not complete, and is subject to modification in any prospectus supplement for any issuance of depositary shares. You should refer to the forms of the deposit agreement, our certificate of incorporation and the certificate of designation that are, or will be, filed with the SEC for the applicable series of preferred stock.

Dividends

The depositary will distribute cash dividends or other cash distributions, if any, received in respect of the series of preferred stock underlying the depositary shares to the record holders of depositary receipts in proportion to the number of depositary shares owned by those holders on the relevant record date. The relevant record date for depositary shares will be the same date as the record date for the preferred stock.

In the event of a distribution other than in cash, the depositary will distribute property received by it to the record holders of depositary receipts that are entitled to receive the distribution, unless the depositary determines that it is not feasible to make the distribution. If this occurs, the depositary, with our approval, may adopt another method for the distribution, including selling the property and distributing the net proceeds to the holders.

Liquidation preference

If a series of preferred stock underlying the depositary shares has a liquidation preference, in the event of our voluntary or involuntary liquidation, dissolution or winding up, holders of depositary shares will be entitled to receive the fraction of the liquidation preference accorded each share of the applicable series of preferred stock, as set forth in the applicable prospectus supplement.

Redemption

If a series of preferred stock underlying the depositary shares is subject to redemption, the depositary shares will be redeemed from the proceeds received by the depositary resulting from the redemption, in whole or in part, of the preferred stock held by the depositary. Whenever we redeem any preferred stock held by the depositary, the depositary will redeem, as of the same redemption date, the number of depositary shares representing the preferred stock so redeemed. The depositary will mail the notice of redemption to the record holders of the depositary receipts promptly upon receiving the notice from us and not fewer than 20 or more than 60 days, unless otherwise provided in the applicable prospectus supplement, prior to the date fixed for redemption of the preferred stock.

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Voting

Upon receipt of notice of any meeting at which the holders of preferred stock are entitled to vote, the depositary will mail the information contained in the notice of meeting to the record holders of the depositary receipts underlying the preferred stock. Each record holder of those depositary receipts on the record date will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the amount of preferred stock underlying that holder's depositary shares. The record date for the depositary will be the same date as the record date for the preferred stock. The depositary will, to the extent practicable, vote the preferred stock underlying the depositary shares in accordance with these instructions. We will agree to take all action that may be deemed necessary by the depositary in order to enable the depositary to vote the preferred stock in accordance with these instructions. The depositary will not vote the preferred stock to the extent that it does not receive specific instructions from the holders of depositary receipts.

Withdrawal of preferred stock

Owners of depositary shares will be entitled to receive upon surrender of depositary receipts at the principal office of the depositary and payment of any unpaid amount due to the depositary, the number of whole shares of preferred stock underlying their depositary shares.

Partial shares of preferred stock will not be issued. Holders of preferred stock will not be entitled to deposit the shares under the deposit agreement or to receive depositary receipts evidencing depositary shares for the preferred stock.

Amendment and termination of the deposit agreement

The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may be amended by agreement between the depositary and us. However, any amendment which materially and adversely alters the rights of the holders of depositary shares, other than fee changes, will not be effective unless the amendment has been approved by at least a majority of the outstanding depositary shares. The deposit agreement may be terminated by the depositary or us only if:

all outstanding depositary shares have been redeemed; or

there has been a final distribution of the preferred stock in connection with our dissolution and such distribution has been made to all the holders of depositary shares.

Charges of depositary

We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangement. We will also pay charges of the depositary in connection with:

the initial deposit of the preferred stock;

the initial issuance of the depositary shares;

any redemption of the preferred stock; and

all withdrawals of preferred stock by owners of depositary shares.

Holders of depositary receipts will pay transfer, income and other taxes and governmental charges and other specified charges as provided in the deposit agreement for their accounts. If these charges have not been paid, the depositary may:

refuse to transfer depositary shares;

withhold dividends and distributions; and

sell the depositary shares evidenced by the depositary receipt.

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Miscellaneous

The depositary will forward to the holders of depositary receipts all reports and communications we deliver to the depositary that we are required to furnish to the holders of the preferred stock. In addition, the depositary will make available for inspection by holders of depositary receipts at the principal office of the depositary, and at such other places as it may from time to time deem advisable, any reports and communications we deliver to the depositary as the holder of preferred stock.

Neither the depositary nor we will be liable if either the depositary or we are prevented or delayed by law or any circumstance beyond the control of either the depositary or us in performing our respective obligations under the deposit agreement. Our obligations and the depositary's obligations will be limited to the performance in good faith of our or the depositary's respective duties under the deposit agreement. Neither the depositary nor we will be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or preferred stock unless satisfactory indemnity is furnished. The depositary and we may rely on:

written advice of counsel or accountants;

information provided by holders of depositary receipts or other persons believed in good faith to be competent to give such information; and

documents believed to be genuine and to have been signed or presented by the proper party or parties.

Resignation and removal of depositary

The depositary may resign at any time by delivering a notice to us. We may remove the depositary at any time. Any such resignation or removal will take effect upon the appointment of a successor depositary and its acceptance of such appointment. The successor depositary must be appointed within 60 days after delivery of the notice for resignation or removal. The successor depositary must be a bank and trust company having its principal office in the United States of America and having a combined capital and surplus of at least \$100,000,000.

Federal income tax consequences

Owners of the depositary shares will be treated for U.S. federal income tax purposes as if they were owners of the preferred stock underlying the depositary shares. As a result, owners will be entitled to take into account for U.S. federal income tax purposes and deductions to which they would be entitled if they were holders of such preferred stock. No gain or loss will be recognized for U.S. federal income tax purposes upon the withdrawal of preferred stock in exchange for depositary shares. The tax basis of each share of preferred stock to an exchanging owner of depositary shares will, upon such exchange, be the same as the aggregate tax basis of the depositary shares exchanged. The holding period for preferred stock in the hands of an exchanging owner of depositary shares will include the period during which such person owned such depositary shares.

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DESCRIPTION OF THE WARRANTS

General

We may issue warrants for the purchase of our debt securities, preferred stock or common stock, or any combination thereof. Warrants may be issued independently or together with our debt securities, preferred stock or common stock and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with the warrants. The warrant agent will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. This summary of certain provisions of the warrants is not complete. For the terms of a particular series of warrants, you should refer to the prospectus supplement for that series of warrants and the warrant agreement for that particular series.

Debt warrants

The prospectus supplement relating to a particular issue of warrants to purchase debt securities will describe the terms of the debt warrants, including the following:

the title of the debt warrants;

the offering price for the debt warrants, if any;

the aggregate number of the debt warrants;

the designation and terms of the debt securities, including any conversion rights, purchasable upon exercise of the debt warrants;

if applicable, the date from and after which the debt warrants and any debt securities issued with them will be separately transferable;

the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;

the dates on which the right to exercise the debt warrants will commence and expire;

if applicable, the minimum or maximum amount of the debt warrants that may be exercised at any one time;

whether the debt warrants represented by the debt warrant certificates or debt securities that may be issued upon exercise of the debt warrants will be issued in registered or bearer form;

information with respect to book-entry procedures, if any; the currency or currency units in which the offering price, if any, and the exercise price are payable;

if applicable, a discussion of material U.S. federal income tax considerations;

the antidilution provisions of the debt warrants, if any;

the redemption or call provisions, if any, applicable to the debt warrants;

any provisions with respect to the holder's right to require us to repurchase the debt warrants upon a change in control or similar event; and

any additional terms of the debt warrants, including procedures, and limitations relating to the exchange, exercise and settlement of the debt warrants.

Debt warrant certificates will be exchangeable for new debt warrant certificates of different denominations. Debt warrants may be exercised at the corporate trust office of the warrant agent or any other office indicated in the prospectus supplement. Prior to the exercise of their debt warrants, holders of debt warrants will not have any of the rights of holders of the debt securities purchasable upon exercise and will not be entitled to payment of principal or any premium, if any, or interest on the debt securities purchasable upon exercise.

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Equity warrants

The prospectus supplement relating to a particular series of warrants to purchase our common stock or preferred stock will describe the terms of the warrants, including the following:

the title of the warrants;

the offering price for the warrants, if any;

the aggregate number of warrants;

the designation and terms of the common stock or preferred stock that may be purchased upon exercise of the warrants;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each security;

if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;

the number of shares of common stock or preferred stock that may be purchased upon exercise of a warrant and the exercise price for the warrants;

the dates on which the right to exercise the warrants shall commence and expire;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

the currency or currency units in which the offering price, if any, and the exercise price are payable;

if applicable, a discussion of material U.S. federal income tax considerations;

the antidilution provisions of the warrants, if any;

the redemption or call provisions, if any, applicable to the warrants;

any provisions with respect to the holder's right to require us to repurchase the warrants upon a change in control or similar event;
and

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any additional terms of the warrants, including procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled:

to vote, consent or receive dividends;

receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or

exercise any rights as stockholders of us.

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DESCRIPTION OF THE DEBT SECURITIES

The debt securities may be either secured or unsecured and will either be our senior debt securities or our subordinated debt securities. The debt securities will be issued under one or more separate indentures between us and a trustee to be specified in an accompanying prospectus supplement. Senior debt securities will be issued under a senior indenture and subordinated debt securities will be issued under a subordinated indenture. Together, the senior indenture and the subordinated indenture are called indentures in this description. This prospectus, together with the applicable prospectus supplement, will describe the terms of a particular series of debt securities.

The following is a summary of selected provisions and definitions of the indentures and debt securities to which any prospectus supplement may relate. The summary of selected provisions of the indentures and the debt securities appearing below is not complete and is subject to, and qualified entirely by reference to, all of the provisions of the applicable indenture and certificates evidencing the applicable debt securities. For additional information, you should look at the applicable indenture and the certificate evidencing the applicable debt security that is filed as an exhibit to the registration statement that includes the prospectus. In this description of the debt securities, the words we, us, or our refer only to Pacific Biosciences of California, Inc. and not to any of our subsidiaries, unless we expressly state or the context otherwise requires.

The following description sets forth selected general terms and provisions of the applicable indenture and debt securities to which any prospectus supplement may relate. Other specific terms of the applicable indenture and debt securities will be described in the applicable prospectus supplement. If any particular terms of the indenture or debt securities described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement.

General

Debt securities may be issued in separate series without limitation as to aggregate principal amount. We may specify a maximum aggregate principal amount for the debt securities of any series.

We are not limited as to the amount of debt securities we may issue under the indentures. Unless otherwise provided in a prospectus supplement, a series of debt securities may be reopened to issue additional debt securities of such series.

The prospectus supplement relating to a particular series of debt securities will set forth:

whether the debt securities are senior or subordinated;

the offering price;

the title;

any limit on the aggregate principal amount;

the person who shall be entitled to receive interest, if other than the record holder on the record date;

the date or dates the principal will be payable;

the interest rate or rates, which may be fixed or variable, if any, the date from which interest will accrue, the interest payment dates and the regular record dates, or the method for calculating the dates and rates;

the place where payments may be made;

any mandatory or optional redemption provisions or sinking fund provisions and any applicable redemption or purchase prices associated with these provisions;

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if issued other than in denominations of U.S. \$1,000 or any multiple of U.S. \$1,000, the denominations in which the debt securities shall be issuable;

if applicable, the method for determining how the principal, premium, if any, or interest will be calculated by reference to an index or formula;

if other than U.S. currency, the currency or currency units in which principal, premium, if any, or interest will be payable and whether we or a holder may elect payment to be made in a different currency;

the portion of the principal amount that will be payable upon acceleration of maturity, if other than the entire principal amount;

if the principal amount payable at stated maturity will not be determinable as of any date prior to stated maturity, the amount or method for determining the amount which will be deemed to be the principal amount;

if applicable, whether the debt securities shall be subject to the defeasance provisions described below under Satisfaction and discharge; defeasance or such other defeasance provisions specified in the applicable prospectus supplement for the debt securities;

any conversion or exchange provisions;

whether the debt securities will be issuable in the form of a global security;

any subordination provisions applicable to the subordinated debt securities if different from those described below under Subordinated debt securities;

any paying agents, authenticating agents, security registrars or other agents for the debt securities, if other than the trustee;

any provisions relating to any security provided for the debt securities, including any provisions regarding the circumstances under which collateral may be released or substituted;

any deletions of, or changes or additions to, the events of default, acceleration provisions or covenants;

any provisions relating to guaranties for the securities and any circumstances under which there may be additional obligors; and

any other specific terms of such debt securities.

Unless otherwise specified in the prospectus supplement, the debt securities will be registered debt securities. Debt securities may be sold at a substantial discount below their stated principal amount, bearing no interest or interest at a rate which at time of issuance is below market rates. The U.S. federal income tax considerations applicable to debt securities sold at a discount will be described in the applicable prospectus

supplement.

Exchange and transfer

Debt securities may be transferred or exchanged at the office of the security registrar or at the office of any transfer agent designated by us.

We will not impose a service charge for any transfer or exchange, but we may require holders to pay any tax or other governmental charges associated with any transfer or exchange.

In the event of any partial redemption of debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange, any debt security of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption and ending at the close of business on the day of the mailing; or

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register the transfer of or exchange any debt security of that series selected for redemption, in whole or in part, except the unredeemed portion being redeemed in part.

We will appoint the trustee as the initial security registrar. Any transfer agent, in addition to the security registrar initially designated by us, will be named in the prospectus supplement. We may designate additional transfer agents or change transfer agents or change the office of the transfer agent. However, we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

Global securities

The debt securities of any series may be represented, in whole or in part, by one or more global securities. Each global security will:

be registered in the name of a depositary, or its nominee, that we will identify in a prospectus supplement;

be deposited with the depositary or nominee or custodian; and

bear any required legends.

No global security may be exchanged in whole or in part for debt securities registered in the name of any person other than the depositary or any nominee unless:

the depositary has notified us that it is unwilling or unable to continue as depositary or has ceased to be qualified to act as depositary;

an event of default is continuing with respect to the debt securities of the applicable series; or

any other circumstance described in a prospectus supplement has occurred permitting or requiring the issuance of any such security. As long as the depositary, or its nominee, is the registered owner of a global security, the depositary or nominee will be considered the sole owner and holder of the debt securities represented by the global security for all purposes under the indentures. Except in the above limited circumstances, owners of beneficial interests in a global security will not be:

entitled to have the debt securities registered in their names;

entitled to physical delivery of certificated debt securities; or

considered to be holders of those debt securities under the indenture.

Payments on a global security will be made to the depositary or its nominee as the holder of the global security. Some jurisdictions have laws that require that certain purchasers of securities take physical delivery of such securities in definitive form. These laws may impair the ability to transfer beneficial interests in a global security.

Institutions that have accounts with the depositary or its nominee are referred to as participants. Ownership of beneficial interests in a global security will be limited to participants and to persons that may hold beneficial interests through participants. The depositary will credit, on its book-entry registration and transfer system, the respective principal amounts of debt securities represented by the global security to the accounts of its participants.

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Ownership of beneficial interests in a global security will be shown on and effected through records maintained by the depositary, with respect to participants' interests, or any participant, with respect to interests of persons held by participants on their behalf.

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Payments, transfers and exchanges relating to beneficial interests in a global security will be subject to policies and procedures of the depository. The depository policies and procedures may change from time to time. Neither any trustee nor we will have any responsibility or liability for the depository's or any participant's records with respect to beneficial interests in a global security.

Payment and paying agents

Unless otherwise indicated in a prospectus supplement, the provisions described in this paragraph will apply to the debt securities. Payment of interest on a debt security on any interest payment date will be made to the person in whose name the debt security is registered at the close of business on the regular record date. Payment on debt securities of a particular series will be payable at the office of a paying agent or paying agents designated by us. However, at our option, we may pay interest by mailing a check to the record holder. The trustee will be designated as our initial paying agent.

We may also name any other paying agents in a prospectus supplement. We may designate additional paying agents, change paying agents or change the office of any paying agent. However, we will be required to maintain a paying agent in each place of payment for the debt securities of a particular series.

All moneys paid by us to a paying agent for payment on any debt security that remain unclaimed for a period ending the earlier of:

10 business days prior to the date the money would be turned over to the applicable state; or

at the end of two years after such payment was due,
will be repaid to us thereafter. The holder may look only to us for such payment.

No protection in the event of a change of control

Unless otherwise indicated in a prospectus supplement with respect to a particular series of debt securities, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction, whether or not such transaction results in a change in control.

Covenants

Unless otherwise indicated in a prospectus supplement with respect to a particular series of debt securities, the debt securities will not contain any financial or restrictive covenants.

Consolidation, merger and sale of assets

Unless we indicate otherwise in a prospectus supplement with respect to a particular series of debt securities, we may not consolidate with or merge into any other person (other than a subsidiary of us), in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to, any person (other than a subsidiary of Pacific Biosciences), unless:

the successor entity, if any, is a U.S. corporation, limited liability company, partnership, trust or other business entity;

the successor entity assumes our obligations on the debt securities and under the indentures;

immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and

certain other conditions specified in the indenture are met.

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Events of default

Unless we indicate otherwise in a prospectus supplement, the following will be events of default for any series of debt securities under the indentures:

- (1) we fail to pay principal of or any premium on any debt security of that series when due;
- (2) we fail to pay any interest on any debt security of that series for 30 days after it becomes due;
- (3) we fail to deposit any sinking fund payment when due;
- (4) we fail to perform any other covenant in the indenture and such failure continues for 90 days after we are given the notice required in the indentures; and
- (5) certain events involving our bankruptcy, insolvency or reorganization.

Additional or different events of default applicable to a series of debt securities may be described in a prospectus supplement. An event of default of one series of debt securities is not necessarily an event of default for any other series of debt securities.

The trustee may withhold notice to the holders of any default, except defaults in the payment of principal, premium, if any, interest, any sinking fund installment on, or with respect to any conversion right of, the debt securities of such series. However, the trustee must consider it to be in the interest of the holders of the debt securities of such series to withhold this notice.

Unless we indicate otherwise in a prospectus supplement, if an event of default, other than an event of default described in clause (5) above, shall occur and be continuing with respect to any series of debt securities, either the trustee or the holders of at least 25 percent in aggregate principal amount of the outstanding securities of that series may declare the principal amount and premium, if any, of the debt securities of that series, or if any debt securities of that series are original issue discount securities, such other amount as may be specified in the applicable prospectus supplement, in each case together with accrued and unpaid interest, if any, thereon, to be due and payable immediately.

Unless we indicate otherwise in a prospectus supplement, if an event of default described in clause (5) above shall occur, the principal amount and premium, if any, of all the debt securities of that series, or if any debt securities of that series are original issue discount securities, such other amount as may be specified in the applicable prospectus supplement, in each case together with accrued and unpaid interest, if any, thereon, will automatically become immediately due and payable. Any payment by us on the subordinated debt securities following any such acceleration will be subject to the subordination provisions described below under Subordinated debt securities.

Notwithstanding the foregoing, each indenture will provide that we may, at our option, elect that the sole remedy for an event of default relating to our failure to comply with our obligations described under the section entitled Reports below or our failure to comply with the requirements of Section 314(a)(1) of the Trust Indenture Act will for the first 180 days after the occurrence of such an event of default consist exclusively of the right to receive additional interest on the relevant series of debt securities at an annual rate equal to (i) 0.25% of the principal amount of such series of debt securities for the first 90 days after the occurrence of such event of default and (ii) 0.50% of the principal amount of such series of debt securities from the 91st day to, and including, the 180th day after the occurrence of such event of default, which we call additional interest. If we so elect, the additional interest will accrue on all outstanding debt securities from and including the date on which such event of default first occurs until such violation is cured or waived and shall be payable on each relevant interest payment date to holders of record on the regular record date immediately preceding the interest payment date. On the 181st day after such event of default (if such violation is not cured or waived prior to such 181st day), the debt securities will be subject to acceleration as provided above. In the event we do not elect to pay additional interest upon any such event of default in accordance with this paragraph, the debt securities will be subject to acceleration as provided above.

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In order to elect to pay the additional interest as the sole remedy during the first 180 days after the occurrence of any event of default relating to the failure to comply with the reporting obligations in accordance with the preceding paragraph, we must notify all holders of debt securities and the trustee and paying agent of such election prior to the close of business on the first business day following the date on which such event of default occurs. Upon our failure to timely give such notice or pay the additional interest, the debt securities will be immediately subject to acceleration as provided above.

After acceleration, the holders of a majority in aggregate principal amount of the outstanding securities of that series may, under certain circumstances, rescind and annul such acceleration if all events of default, other than the non-payment of accelerated principal, or other specified amounts or interest, have been cured or waived.

Other than the duty to act with the required care during an event of default, the trustee will not be obligated to exercise any of its rights or powers at the request of the holders unless the holders shall have offered to the trustee reasonable indemnity. Generally, the holders of a majority in aggregate principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee.

A holder of debt securities of any series will not have any right to institute any proceeding under the indentures, or for the appointment of a receiver or a trustee, or for any other remedy under the indentures, unless:

- (1) the holder has previously given to the trustee written notice of a continuing event of default with respect to the debt securities of that series;
 - (2) the holders of at least 25 percent in aggregate principal amount of the outstanding debt securities of that series have made a written request and have offered reasonable indemnity to the trustee to institute the proceeding; and
 - (3) the trustee has failed to institute the proceeding and has not received direction inconsistent with the original request from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series within 60 days after the original request.
- Holders may, however, sue to enforce the payment of principal, premium or interest on any debt security on or after the due date or to enforce the right, if any, to convert any debt security (if the debt security is convertible) without following the procedures listed in (1) through (3) above.

We will furnish the trustee an annual statement from our officers as to whether or not we are in default in the performance of the conditions and covenants under the indenture and, if so, specifying all known defaults.

Modification and waiver

Unless we indicate otherwise in a prospectus supplement, the applicable trustee and we may make modifications and amendments to an indenture with the consent of the holders of a majority in aggregate principal amount of the outstanding securities of each series affected by the modification or amendment.

We may also make modifications and amendments to the indentures for the benefit of holders without their consent, for certain purposes including, but not limited to:

providing for our successor to assume the covenants under the indenture;

adding covenants or events of default;

making certain changes to facilitate the issuance of the securities;

securing the securities;

providing for a successor trustee or additional trustees;

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conforming the indenture to the description of the debt securities set forth in this prospectus or the accompanying prospectus supplement;

curing any ambiguities or inconsistencies;

providing for guaranties of, or additional obligors on, the securities;

permitting or facilitating the defeasance and discharge of the securities; and

other changes specified in the indenture.

However, neither the trustee nor we may make any modification or amendment without the consent of the holder of each outstanding security of that series affected by the modification or amendment if such modification or amendment would:

change the stated maturity of any debt security;

reduce the principal, premium, if any, or interest on any debt security or any amount payable upon redemption or repurchase, whether at our option or the option of any holder, or reduce the amount of any sinking fund payments;

reduce the principal of an original issue discount security or any other debt security payable on acceleration of maturity;

change the place of payment or the currency in which any debt security is payable;

impair the right to enforce any payment after the stated maturity or redemption date;

if subordinated debt securities, modify the subordination provisions in a materially adverse manner to the holders;

adversely affect the right to convert any debt security if the debt security is a convertible debt security; or

change the provisions in the indenture that relate to modifying or amending the indenture.

Satisfaction and discharge; defeasance

We may be discharged from our obligations on the debt securities, subject to limited exceptions, of any series that have matured or will mature or be redeemed within one year if we deposit enough money with the trustee to pay all the principal, interest and any premium due to the stated maturity date or redemption date of the debt securities.

Each indenture contains a provision that permits us to elect either or both of the following:

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We may elect to be discharged from all of our obligations, subject to limited exceptions, with respect to any series of debt securities then outstanding. If we make this election, the holders of the debt securities of the series will not be entitled to the benefits of the indenture, except for the rights of holders to receive payments on debt securities or the registration of transfer and exchange of debt securities and replacement of lost, stolen or mutilated debt securities.

We may elect to be released from our obligations under some or all of any financial or restrictive covenants applicable to the series of debt securities to which the election relates and from the consequences of an event of default resulting from a breach of those covenants.

To make either of the above elections, we must irrevocably deposit in trust with the trustee enough money to pay in full the principal, interest and premium on the debt securities. This amount may be made in cash and/or U.S. government obligations or, in the case of debt securities denominated in a currency other than U.S. dollars, cash in the currency in which such series of securities is denominated and/or foreign government obligations. As

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a condition to either of the above elections, for debt securities denominated in U.S. dollars we must deliver to the trustee an opinion of counsel that the holders of the debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the action.

With respect to debt securities of any series that are denominated in a currency other than United States dollars, foreign government obligations means:

direct obligations of the government that issued or caused to be issued the currency in which such securities are denominated and for the payment of which obligations its full faith and credit is pledged, or, with respect to debt securities of any series which are denominated in Euros, direct obligations of certain members of the European Union for the payment of which obligations the full faith and credit of such members is pledged, which in each case are not callable or redeemable at the option of the issuer thereof; or

obligations of a person controlled or supervised by or acting as an agency or instrumentality of a government described in the bullet above the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by such government, which are not callable or redeemable at the option of the issuer thereof.

Reports

The indentures provide that any reports or documents that we file with the SEC pursuant to Section 13 or 15(d) of the Exchange Act will be filed with the trustee within 15 days after the same is filed with the SEC. Documents filed by us with the SEC via the EDGAR system will be deemed filed with the trustee as of the time such documents are filed with the SEC.

Notices

Notices to holders will be given by mail to the addresses of the holders in the security register.

Governing law

The indentures and the debt securities will be governed by, and construed under, the laws of the State of New York.

No personal liability of directors, officers, employees and stockholders

No incorporator, stockholder, employee, agent, officer, director or subsidiary of ours will have any liability for any obligations of ours, or because of the creation of any indebtedness under the debt securities, the indentures or supplemental indentures. The indentures provide that all such liability is expressly waived and released as a condition of, and as a consideration for, the execution of such indentures and the issuance of the debt securities.

Regarding the trustee

The indentures limit the right of the trustee, should it become our creditor, to obtain payment of claims or secure its claims.

The trustee will be permitted to engage in certain other transactions with us. However, if the trustee acquires any conflicting interest, and there is a default under the debt securities of any series for which it is trustee, the trustee must eliminate the conflict or resign.

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Subordinated debt securities

The following provisions will be applicable with respect to each series of subordinated debt securities, unless otherwise stated in the prospectus supplement relating to that series of subordinated debt securities.

The indebtedness evidenced by the subordinated debt securities of any series is subordinated, to the extent provided in the subordinated indenture and the applicable prospectus supplement, to the prior payment in full, in cash or other payment satisfactory to the holders of senior debt, of all senior debt, including any senior debt securities.

Upon any distribution of our assets upon any dissolution, winding up, liquidation or reorganization, whether voluntary or involuntary, marshalling of assets, assignment for the benefit of creditors, or in bankruptcy, insolvency, receivership or other similar proceedings, payments on the subordinated debt securities will be subordinated in right of payment to the prior payment in full in cash or other payment satisfactory to holders of senior debt of all senior debt.

In the event of any acceleration of the subordinated debt securities of any series because of an event of default with respect to the subordinated debt securities of that series, holders of any senior debt would be entitled to payment in full in cash or other payment satisfactory to holders of senior debt of all senior debt before the holders of subordinated debt securities are entitled to receive any payment or distribution.

In addition, the subordinated debt securities will be structurally subordinated to all indebtedness and other liabilities of our subsidiaries, including trade payables and lease obligations. This occurs because our right to receive any assets of our subsidiaries upon their liquidation or reorganization, and your right to participate in those assets, will be effectively subordinated to the claims of that subsidiary's creditors, including trade creditors, except to the extent that we are recognized as a creditor of such subsidiary. If we are recognized as a creditor of that subsidiary, our claims would still be subordinate to any security interest in the assets of the subsidiary and any indebtedness of the subsidiary senior to us.

We are required to promptly notify holders of senior debt or their representatives under the subordinated indenture if payment of the subordinated debt securities is accelerated because of an event of default.

Under the subordinated indenture, we may also not make payment on the subordinated debt securities if:

a default in our obligations to pay principal, premium, if any, interest or other amounts on our senior debt occurs and the default continues beyond any applicable grace period, which we refer to as a payment default; or

any other default occurs and is continuing with respect to designated senior debt that permits holders of designated senior debt to accelerate its maturity, which we refer to as a non-payment default, and the trustee receives a payment blockage notice from us or some other person permitted to give the notice under the subordinated indenture.

We will resume payments on the subordinated debt securities:

in case of a payment default, when the default is cured or waived or ceases to exist, and

in case of a nonpayment default, the earlier of when the default is cured or waived or ceases to exist or 179 days after the receipt of the payment blockage notice.

No new payment blockage period may commence on the basis of a nonpayment default unless 365 days have elapsed from the effectiveness of the immediately prior payment blockage notice. No nonpayment default that existed or was continuing on the date of delivery of any payment blockage notice to the trustee shall be the basis for a subsequent payment blockage notice.

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As a result of these subordination provisions, in the event of our bankruptcy, dissolution or reorganization, holders of senior debt may receive more, ratably, and holders of the subordinated debt securities may receive less, ratably, than our other creditors. The subordination provisions will not prevent the occurrence of any event of default under the subordinated indenture.

The subordination provisions will not apply to payments from money or government obligations held in trust by the trustee for the payment of principal, interest and premium, if any, on subordinated debt securities pursuant to the provisions described under the section entitled Satisfaction and discharge; defeasance, if the subordination provisions were not violated at the time the money or government obligations were deposited into trust.

If the trustee or any holder receives any payment that should not have been made to them in contravention of subordination provisions before all senior debt is paid in full in cash or other payment satisfactory to holders of senior debt, then such payment will be held in trust for the holders of senior debt.

Senior debt securities will constitute senior debt under the subordinated indenture.

Additional or different subordination provisions may be described in a prospectus supplement relating to a particular series of debt securities.

Definitions

Designated senior debt means our obligations under any particular senior debt in which the instrument creating or evidencing the same or the assumption or guarantee thereof, or related agreements or documents to which we are a party, expressly provides that such indebtedness shall be designated senior debt for purposes of the subordinated indenture. The instrument, agreement or other document evidencing any designated senior debt may place limitations and conditions on the right of such senior debt to exercise the rights of designated senior debt.

Indebtedness means the following, whether absolute or contingent, secured or unsecured, due or to become due, outstanding on the date of the indenture for such series of securities or thereafter created, incurred or assumed:

our indebtedness evidenced by a credit or loan agreement, note, bond, debenture or other written obligation;

all of our obligations for money borrowed;

all of our obligations evidenced by a note or similar instrument given in connection with the acquisition of any businesses, properties or assets of any kind,

our obligations:

as lessee under leases required to be capitalized on the balance sheet of the lessee under generally accepted accounting principles, or

as lessee under leases for facilities, capital equipment or related assets, whether or not capitalized, entered into or leased for financing purposes;

all of our obligations under interest rate and currency swaps, caps, floors, collars, hedge agreements, forward contracts or similar agreements or arrangements;

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all of our obligations with respect to letters of credit, bankers' acceptances and similar facilities, including reimbursement obligations with respect to the foregoing;

all of our obligations issued or assumed as the deferred purchase price of property or services, but excluding trade accounts payable and accrued liabilities arising in the ordinary course of business;

all obligations of the type referred to in the above clauses of another person, the payment of which, in either case, we have assumed or guaranteed, for which we are responsible or liable, directly or indirectly, jointly or severally, as obligor, guarantor or otherwise, or which are secured by a lien on our property; and

renewals, extensions, modifications, replacements, restatements and refundings of, or any indebtedness or obligation issued in exchange for, any such indebtedness or obligation described in the above clauses of this definition.

Senior debt means the principal of, premium, if any, and interest, including all interest accruing subsequent to the commencement of any bankruptcy or similar proceeding, whether or not a claim for post-petition interest is allowable as a claim in any such proceeding, and rent payable on or in connection with, and all fees and other amounts payable in connection with, our indebtedness. However, senior debt shall not include:

any debt or obligation if its terms or the terms of the instrument under which or pursuant to which it is issued expressly provide that it shall not be senior in right of payment to the subordinated debt securities or expressly provide that such indebtedness is on the same basis or junior to the subordinated debt securities; or

debt to any of our subsidiaries, a majority of the voting stock of which is owned, directly or indirectly, by us.

Subsidiary means a corporation more than 50% of the outstanding voting stock of which is owned, directly or indirectly, by us or by one or more of our other subsidiaries or by a combination of us and our other subsidiaries. For purposes of this definition, voting stock means stock or other similar interests which ordinarily has or have voting power for the election of directors, or persons performing similar functions, whether at all times or only so long as no senior class of stock or other interests has or have such voting power by reason of any contingency.

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DESCRIPTION OF THE UNITS

We may issue units comprised of one or more of the other classes of securities described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The units may be issued under unit agreements to be entered into between us and a unit agent, as detailed in the prospectus supplement relating to the units being offered. The prospectus supplement will describe:

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances the securities comprising the units may be held or transferred separately;

a description of the terms of any unit agreement governing the units;

a description of the provisions for the payment, settlement, transfer or exchange of the units;

a discussion of material federal income tax considerations, if applicable; and

whether the units if issued as a separate security will be issued in fully registered or global form.

The descriptions of the units in this prospectus and in any prospectus supplement are summaries of the material provisions of the applicable agreements. These descriptions do not restate those agreements in their entirety and may not contain all the information that you may find useful. We urge you to read the applicable agreements because they, and not the summaries, define your rights as holders of the units. For more information, please review the forms of the relevant agreements, which will be filed with the SEC promptly after the offering of units and will be available as described under the heading **Where You Can Find More Information**.

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PLAN OF DISTRIBUTION

We may sell the securities offered through this prospectus (1) to or through underwriters or dealers, (2) directly to purchasers, including our affiliates, (3) through agents, or (4) through a combination of any these methods. The securities may be distributed at a fixed price or prices, which may be changed, market prices prevailing at the time of sale, prices related to the prevailing market prices, or negotiated prices. The prospectus supplement will include the following information:

the terms of the offering;

the names of any underwriters or agents;

the name or names of any managing underwriter or underwriters;

the purchase price of the securities;

the net proceeds from the sale of the securities;

any delayed delivery arrangements;

any underwriting discounts, commissions and other items constituting underwriters' compensation;

any initial public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any commissions paid to agents.

Sale through underwriters or dealers

If underwriters are used in the sale, the underwriters will acquire the securities for their own account, including through underwriting, purchase, security lending or repurchase agreements with us. The underwriters may resell the securities from time to time in one or more transactions, including negotiated transactions. Underwriters may sell the securities in order to facilitate transactions in any of our other securities (described in this prospectus or otherwise), including other public or private transactions and short sales. Underwriters may offer securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless otherwise indicated in the prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions, and the underwriters will be obligated to purchase all the offered securities if they purchase any of them. The underwriters may change from time to time any initial public offering price and any discounts or concessions allowed or reallocated or paid to dealers. The prospectus supplement will include the names of the principal underwriters, the respective amount of securities underwritten, the nature of the obligation of the underwriters to take the securities and the nature of any material relationship between an underwriter and us.

If dealers are used in the sale of securities offered through this prospectus, we will sell the securities to them as principals. They may then resell those securities to the public at varying prices determined by the dealers at the time of resale. The prospectus supplement will include the names of the dealers and the terms of the transaction.

Direct sales and sales through agents

We may sell the securities offered through this prospectus directly. In this case, no underwriters or agents would be involved. Such securities may also be sold through agents designated from time to time. The prospectus supplement will name any agent involved in the offer or sale of the offered securities and will describe any commissions payable to the agent by us. Unless otherwise indicated in the prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment.

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We may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities. The terms of any such sales will be described in the prospectus supplement.

Market making, stabilization and other transactions

Unless the applicable prospectus supplement states otherwise, each series of offered securities will be a new issue and will have no established trading market. We may elect to list any series of offered securities on an exchange. Any underwriters that we use in the sale of offered securities may make a market in such securities, but may discontinue such market making at any time without notice. Therefore, we cannot assure you that the securities will have a liquid trading market.

Any underwriter may also engage in stabilizing transactions, syndicate covering transactions and penalty bids in accordance with Rule 104 under the Securities Exchange Act of 1934, as amended. Stabilizing transactions involve bids to purchase the underlying security in the open market for the purpose of pegging, fixing or maintaining the price of the securities. Syndicate covering transactions involve purchases of the securities in the open market after the distribution has been completed in order to cover syndicate short positions.

Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when the securities originally sold by the syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. Stabilizing transactions, syndicate covering transactions and penalty bids may cause the price of the securities to be higher than it would be in the absence of the transactions. The underwriters may, if they commence these transactions, discontinue them at any time.

Derivative transactions and hedging

We, the underwriters or other agents may engage in derivative transactions involving the securities. These derivatives may consist of short sale transactions and other hedging activities. The underwriters or agents may acquire a long or short position in the securities, hold or resell securities acquired and purchase options or futures on the securities and other derivative instruments with returns linked to or related to changes in the price of the securities. In order to facilitate these derivative transactions, we may enter into security lending or repurchase agreements with the underwriters or agents. The underwriters or agents may effect the derivative transactions through sales of the securities to the public, including short sales, or by lending the securities in order to facilitate short sale transactions by others. The underwriters or agents may also use the securities purchased or borrowed from us or others (or, in the case of derivatives, securities received from us in settlement of those derivatives) to directly or indirectly settle sales of the securities or close out any related open borrowings of the securities.

Electronic auctions

We may also make sales through the Internet or through other electronic means. Since we may from time to time elect to offer securities directly to the public, with or without the involvement of agents, underwriters or dealers, utilizing the Internet or other forms of electronic bidding or ordering systems for the pricing and allocation of such securities, you should pay particular attention to the description of that system we will provide in a prospectus supplement.

Such electronic system may allow bidders to directly participate, through electronic access to an auction site, by submitting conditional offers to buy that are subject to acceptance by us, and which may directly affect the price or other terms and conditions at which such securities are sold. These bidding or ordering systems may present to each bidder, on a so-called "real-time" basis, relevant information to assist in making a bid, such as the clearing spread at which the offering would be sold, based on the bids submitted, and whether a bidder's individual bids would be accepted, prorated or rejected. For example, in the case of a debt security, the clearing spread could be indicated as a number of basis points above an index treasury note. Of course, many pricing methods can and may also be used.

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Upon completion of such an electronic auction process, securities will be allocated based on prices bid, terms of bid or other factors. The final offering price at which securities would be sold and the allocation of securities among bidders would be based in whole or in part on the results of the Internet or other electronic bidding process or auction.

General information

Agents, underwriters, and dealers may be entitled, under agreements entered into with us, to indemnification by us against certain liabilities, including liabilities under the Securities Act.

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LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2011, and the effectiveness of our internal control over financial reporting as of December 31, 2011, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and our management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2011 are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

The consolidated financial statements incorporated in this S-3 by reference to the Annual Report on Form 10-K for the year ended December 31, 2011 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other 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, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge through the Internet. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

We have filed with the SEC a registration statement under the Securities Act of 1933 relating to the offering of these securities. The registration statement, including the attached exhibits, contains additional relevant information about us and the securities. This prospectus does not contain all of the information set forth in the registration statement. You can obtain a copy of the registration statement, at prescribed rates, from the SEC at the address listed above. The registration statement and the documents referred to below under "Incorporation by Reference" are also available on our Internet website, www.pacificbiosciences.com. We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this prospectus.

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INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus certain information we file with it, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information that we file later with the SEC will automatically update and supersede information contained in this prospectus and any accompanying prospectus supplement. We incorporate by reference the documents listed below that we have previously filed with the SEC (excluding any portions of any Form 8-K that are not deemed filed pursuant to the General Instructions of Form 8-K):

Annual Report on Form 10-K for the fiscal year ended December 31, 2011, including the information specifically incorporated by reference into the Form 10-K from our definitive proxy statement for the 2012 Annual Meeting of Stockholders;

Current Reports on Form 8-K filed January 6, 2012 and January 20, 2012; and

The description of our common stock contained in the Registration Statement on Form 8-A relating thereto, including any amendment or report filed for the purpose of updating such description.

We also incorporate by reference into this prospectus additional documents that we may file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the completion or termination of the offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information deemed furnished and not filed with the SEC. Any statements contained in a previously filed document incorporated by reference into this prospectus is deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus, or in a subsequently filed document also incorporated by reference herein, modifies or supersedes that statement.

This prospectus may contain information that updates, modifies or is contrary to information in one or more of the documents incorporated by reference in this prospectus. You should rely only on the information incorporated by reference or provided in this prospectus. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus is accurate as of any date other than the date of this prospectus or the date of the documents incorporated by reference in this prospectus.

We will provide to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, at no cost to the requester, a copy of any and all of the information that is incorporated by reference in this prospectus.

Requests for such documents should be directed to:

Pacific Biosciences of California, Inc.

1380 Willow Road

Menlo Park, California 94025

Attn: Investor Relations

You may also access the documents incorporated by reference in this prospectus through our website at www.pacificbiosciences.com. Except for the specific incorporated documents listed above, no information available on or through our website shall be deemed to be incorporated in this prospectus or the registration statement of which it forms a part.

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**Up to \$30,000,000 of Shares
Common Stock**

Prospectus Supplement

November 12, 2013