UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of
The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported)
February 2, 2017

Pacific Biosciences of California, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-34899**	**16-1590339**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

1305 O'Brien Drive
Menlo Park, California 94025
(Address of principal executive offices, including zip code)

(650) 521-8000
(Registrant's telephone number, including area code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2):

- o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

ITEM 8.01. OTHER EVENTS

On February 2, 2017, Pacific Biosciences of California, Inc. (the "Company") announced its intention to offer and sell up to an aggregate offering price of $60,000,000 of shares of its common stock, par value $0.001 per share (the "Shares"), from time to time, through an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended (the "Securities Act"). Cantor Fitzgerald & Co. ("Cantor") will act as sales agent for the Shares pursuant to that certain Controlled Equity Offering℠ Sales Agreement, dated October 5, 2012 as amended on November 8, 2013, as further amended on February 3, 2015 (as amended, the "Agreement"), by and between the Company and Cantor. Such aggregate value of Shares is in addition to the shares previously sold pursuant to the Agreement. The Company intends to use the proceeds of the offering for general corporate purposes, including capital expenditures and working capital.

Pursuant to the Agreement, Cantor may sell the Shares by methods deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act, including sales made directly on or through The NASDAQ Global Select Market or on any other existing trading market for the Shares. In addition, pursuant to the Agreement, Cantor may sell the Shares by any other method permitted by law, including in negotiated transactions at market prices prevailing at the time of sale, with the Company's prior consent. Subject to the terms and conditions of the Agreement, Cantor will use commercially reasonable efforts, consistent with its normal trading and sales practices and applicable state and federal law, rules and regulations and the rules of The NASDAQ Global Select Market, to sell the Shares from time to time, based upon the Company's instructions (including any price, time or size limits or other customary parameters or conditions the Company may impose); provided, however, that in no event shall the Company issue or sell through Cantor such number or dollar amount of Shares that would (a) exceed the number or dollar amount of shares of common stock registered on an effective Registration Statement on Form S-3 pursuant to which the offering is being made, (b) exceed the number of authorized but unissued shares of the Company's common stock, (c) exceed the number or dollar amount of shares of the Company's common stock permitted to be sold under a Registration Statement on Form S-3 (including General Instruction I.B.6 thereof, if applicable) or (d) exceed the number or dollar amount of shares of the Company's common stock for which the Company has filed a prospectus supplement to register the shares. The Company is not obligated to make any sales of the Shares under the Agreement. The offering of Shares pursuant to the Agreement will terminate upon the earlier of (a) the sale of all of the Shares subject to the Agreement or (b) the termination of the Agreement by Cantor or the Company.

The Company will pay Cantor a commission of 3.0% of the gross sales price per share sold and has agreed to provide Cantor with customary indemnification and contribution rights.

The Shares will be issued pursuant to the Company's previously filed and effective Registration Statement on Form S-3 (File No. 333-199891), the base prospectus, dated November 21, 2014, filed as part of such Registration Statement, and the prospectus supplement, dated February 2, 2017, filed by the Company with the Securities and Exchange Commission.

This Current Report on Form 8-K shall not constitute an offer to sell or the solicitation of an offer to buy nor shall there be any sale of the Shares in any state in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state.

The Company's unaudited Consolidated Balance Sheets, Consolidated Statements of Operations and Comprehensive Loss and Consolidated Statements of Cash Flows are filed herewith as Exhibit 99.1 and incorporated herein by reference.

The Company has updated its disclosure regarding its Management's Discussion and Analysis of Financial Condition and Results of Operations, Business and Risk Factors. The revised disclosure is filed herewith as Exhibit 99.2 and incorporated herein by reference.

The information set forth in this Item 8.01, as well as Exhibits 99.1 and 99.2 referenced therein, shall be deemed "filed" for purposes of the Securities Exchange Act of 1934, as amended, and shall be incorporated by reference into the Company's filings under the Securities Act of 1933, as amended.

ITEM 9.01. FINANCIAL STATEMENTS AND EXHIBITS.

(d) Exhibits.

5.1	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation.
23.1	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in Exhibit 5.1).
99.1	Consolidated Balance Sheets (unaudited), Consolidated Statements of Operations and Comprehensive Loss (unaudited) and Consolidated Statements of Cash Flows (unaudited).
99.2	Management's Discussion and Analysis of Financial Condition and Results of Operations, Business and Risk Factors.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Pacific Biosciences of California, Inc.

By: /s/ Susan K. Barnes

Susan K. Barnes
Executive Vice President, Chief Financial Officer & Principal Accounting Officer

Date: February 2, 2017

EXHIBIT INDEX

Exhibit No.	Description
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99.2	Management's Discussion and Analysis of Financial Condition and Results of Operations, Business and Risk Factors.

Exhibit 5.1

February 2, 2017

Pacific Biosciences of California, Inc.
1305 O'Brien Drive
Menlo Park, CA 94025

Re: Registration Statement on Form S-3

Ladies and Gentlemen:

We have acted as counsel to Pacific Biosciences of California, Inc., a Delaware corporation (the ***"Company"***), in connection with preparation and filing of a Registration Statement on Form S-3 (File No. 333-199891) (the ***"Registration Statement***") with the Securities and Exchange Commission (the ***"Commission"***) pursuant to the Securities Act of 1933, as amended (the ***"Securities Act"***), and the Prospectus Supplement filed pursuant to Rule 424(b) under the Securities Act, dated February 2, 2017 (the ***"Prospectus Supplement"***), relating to the sale by the Company of shares of its common stock, par value $0.001 per share (the ***"Common Stock"***) having an aggregate offering price of up to $60,000,000 (the ***"Shares"***).

The offering and sale of the Shares are being made pursuant to that certain Controlled Equity Offering℠ Sales Agreement dated as of October 5, 2012, as amended by Amendment No. 1 dated as of November 8, 2013, as further amended by Amendment No. 2 dated as of February 3, 2015 (as amended, the ***"Sales Agreement"***), by and between the Company and Cantor Fitzgerald & Co. (***"Cantor"***).

We have examined copies of the Sales Agreement, the Registration Statement and the Prospectus Supplement. We have also examined instruments, documents and records which we deem relevant and necessary for the basis of our opinion hereinafter expressed. In such examination, we have assumed (i) the authenticity of original documents and the genuineness of all signatures, (ii) the conformity to the originals of all documents submitted to us as copies, and (iii) the truth, accuracy, and completeness of the information, representations and warranties contained in the records, documents, instruments and certificates we have reviewed.

Based on and subject to the foregoing, we are of the opinion that the Shares have been duly authorized by the Company, and when issued and delivered by the Company against payment therefor in accordance with the terms of the Sales Agreement, will be validly issued, fully paid and nonassessable.

We express no opinion as to the laws of any other jurisdiction other than the federal laws of the United States of America and the General Corporation Law of the State of Delaware.

We hereby consent to the use of this opinion as an exhibit to the Company's Current Report on Form 8-K, filed on or about February 2, 2017, for incorporation by reference into the Registration Statement. In giving our consent, we do not believe that we are "experts" within the meaning of such term as used in the Securities Act or the rules and regulations of the Commission issued thereunder with respect to any part of the Registration Statement, including this opinion as an exhibit.

Sincerely,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

/s/ Wilson Sonsini Goodrich & Rosati,
Professional Corporation

Exhibit 99.1

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

Consolidated Balance Sheets
(unaudited)

(in thousands, except per share amounts)	December 31, 2016	December 31, 2015
Assets		
Current assets		
Cash and cash equivalents	$ 16,765	$ 33,629
Investments	55,213	48,641
Accounts receivable	11,421	5,245
Inventory	15,634	10,955
Prepaid expenses and other current assets	9,978	12,071
Total current assets	109,011	110,541
Property and equipment, net	14,560	8,548
Long-term restricted cash	4,500	4,500
Other long-term assets	9,813	7,518
Total assets	$ 137,884	$ 131,107
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$ 8,359	$ 4,749
Accrued expenses	16,604	15,551
Deferred service revenue, current	7,130	6,815
Deferred contractual revenue, current	—	10,822
Other liabilities, current	1,681	241
Total current liabilities	33,774	38,178
Deferred service revenue, non-current	1,297	1,143
Deferred contractual revenue, non-current	—	1,312
Other liabilities, non-current	1,683	1,386
Notes payable	16,106	14,948
Financing derivative	356	600
Total liabilities	53,216	57,567
Commitments and contingencies		
Stockholders' equity		
Preferred Stock, $0.001 par value:		
Authorized 50,000 shares; No shares issued or outstanding	—	—
Common Stock, $0.001 par value:		
Authorized 1,000,000 shares; Issued and outstanding 92,677 and 79,983 shares at December 31, 2016 and 2015, respectively	93	80
Additional paid-in-capital	872,114	786,636
Accumulated other comprehensive income (loss)	5	(7)
Accumulated deficit	(787,544)	(713,169)
Total stockholders' equity	84,668	73,540
Total liabilities and stockholders' equity	$ 137,884	$ 131,107

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

Consolidated Statements of Operations and Comprehensive Loss
(unaudited)

(in thousands, except per share amounts)	Years ended December 31, 2016	2015	2014
Revenue:			
Product revenue	$ 64,609	$ 37,502	$ 35,299
Service and other revenue	13,971	10,896	8,511
Contractual revenue	12,134	44,384	16,784
Total revenue	90,714	92,782	60,594
Cost of Revenue:			
Cost of product revenue	34,512	30,704	29,626
Cost of service and other revenue	12,042	8,628	7,566
Total cost of revenue	46,554	39,332	37,192
Gross profit	44,160	53,450	23,402
Operating Expense:			
Research and development	67,617	60,440	48,230
Sales, general and administrative	47,787	45,187	38,026
Gain on lease amendments	—	(23,043)	—
Total operating expense	115,404	82,584	86,256
Operating loss	(71,244)	(29,134)	(62,854)
Interest expense	(3,234)	(2,926)	(2,828)
Other income (expense), net	103	364	(478)
Net loss	(74,375)	(31,696)	(66,160)
Other comprehensive loss:			
Unrealized gain (loss) on investments	12	(16)	(5)
Comprehensive loss	$ (74,363)	$ (31,712)	$ (66,165)
Net loss per share:			
Basic and diluted net loss per share	$ (0.83)	$ (0.42)	$ (0.94)
Shares used in computing basic and diluted net loss per share	89,148	75,614	70,475

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

Consolidated Statements of Cash Flows
(unaudited)

(in thousands)	Years Ended December 31, 2016	2015	2014
Cash flows from operating activities			
Net loss	$ (74,375)	$ (31,696)	$ (66,160)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization	3,875	3,677	4,221
Amortization of debt discount and financing costs	1,158	957	793
Stock-based compensation	19,562	13,840	9,943
Non-cash portion of gain on lease amendments	—	(3,043)	—
Other items	(147)	(230)	507
Changes in assets and liabilities			
Accounts receivable	(6,176)	(1,738)	(660)
Inventory	(6,151)	(2,466)	(1,285)
Prepaid expenses and other assets	(202)	(17,889)	(224)
Accounts payable	3,402	(716)	3,891
Accrued expenses	1,053	5,732	3,536
Deferred service revenue	469	708	2,686
Deferred contractual revenue	(12,134)	(14,386)	(6,784)
Other liabilities	1,737	(639)	(1,932)
Net cash used in operating activities	(67,929)	(47,889)	(51,468)
Cash flows from investing activities			
Purchase of property and equipment	(8,207)	(3,009)	(1,609)
Proceeds from disposal of property and equipment	10	36	—
Long-term restricted cash	—	(4,500)	—
Purchase of investments	(95,848)	(84,579)	(126,413)
Sales of investments	23,285	8,317	—
Maturities of investments	65,896	92,341	147,586
Net cash provided by (used in) investing activities	(14,864)	8,606	19,564
Cash flows from financing activities			
Proceeds from issuance of common stock from equity plans	7,729	7,363	3,968
Proceeds from issuance of common stock from "at-the-market" offering, net of issuance costs	58,200	29,100	38,023
Net cash provided by financing activities	65,929	36,463	41,991
Net increase (decrease) in cash and cash equivalents	(16,864)	(2,820)	10,087
Cash and cash equivalents at beginning of period	33,629	36,449	26,362
Cash and cash equivalents at end of period	$ 16,765	$ 33,629	$ 36,449
Supplemental disclosure of cash flow information			
Interest paid	$ 1,799	$ 1,794	$ 1,794
Supplemental disclosure of non-cash investing and financing activities			
Inventory transferred to property and equipment	1,282	2,846	—

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Discussions under the captions "Management's Discussion and Analysis of Financial Condition and Results of Operations," "Business" and "Risk Factors," contain or may contain forward-looking statements that are based on the beliefs and assumptions of the management of Pacific Biosciences of California, Inc. (the "Company," "we," "us," or "our") and on information currently available to our management. The statements contained in this Current Report on Form 8-K that are not purely historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and include, but are not limited to, our statements regarding the attributes and sequencing advantages of SMRT® technology and the Sequel™ System, market opportunities, strategic plans, including strategy for our business and related financing, expectations regarding the conversion of backlog to revenue and the pricing and gross margin for products, expectations regarding our collaboration agreements, manufacturing plans including scaling of manufacturing of Sequel Systems and delivery of products, research and development plans, product development including, among other things, statements relating to future uses, quality or performance of, or benefits of using, products or technologies, updates or improvements of our products, intentions regarding seeking regulatory approval for our products, competition, expectations regarding unrecognized income tax benefits, expectations regarding the impact of an increase in market rates on the value of our investment portfolio, the sufficiency of cash, cash equivalents and investments to fund projected operating requirements, the effects of recent accounting pronouncements on our financial statements and other future events. Such statements may be signified by terms such as "anticipates," "believes," "could," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "projects," "seeks," "should," "target," "will," "would" or similar expressions and the negatives of those terms. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed under the heading "Risk Factors" in this report and in other documents we file with the Securities and Exchange Commission ("SEC"). Given these risks and uncertainties, you should not place undue reliance on forward-looking statements. Also, forward-looking statements represent management's beliefs and assumptions as of the date of this report. Except as required by law, we assume no obligation to update forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

We design, develop and manufacture sequencing systems to help scientists resolve genetically complex problems. Based on our novel Single Molecule, Real-Time (SMRT®) Sequencing technology, our products enable: *de novo* genome assembly to finish genomes in order to more fully identify, annotate and decipher genomic structures; full-length transcript analysis to improve annotations in reference genomes, characterize alternatively spliced isoforms in important gene families, and find novel genes; targeted sequencing to more comprehensively characterize genetic variations; and real-time kinetic information for epigenome characterization. Our technology provides high accuracy, ultra-long reads, uniform coverage, and is the only DNA sequencing technology that provides the ability to simultaneously detect epigenetic changes. PacBio® sequencing systems, including consumables and software, provide a simple, fast, end-to-end workflow for SMRT Sequencing.

In September 2015, we announced that we had launched a new nucleic acid sequencing platform, the Sequel™ System, which provides higher throughput, more scalability, a reduced footprint and lower sequencing project costs compared to the PacBio® RS II System, while maintaining the existing benefits of our SMRT Sequencing Technology.

Business Events

Product Developments.

In September 2015, we announced a new nucleic acid sequencing platform, the Sequel System, which provides higher throughput, more scalability, a reduced footprint and lower sequencing project costs compared to the PacBio RS II System, while maintaining the existing benefits of our SMRT Technology. The core of the Sequel System is the capacity of its redesigned SMRT Cells, which contain approximately one million zero-mode waveguides (ZMWs) at launch, compared to approximately 150,000 ZMWs in the PacBio RS II System. We began limited shipments of the Sequel System in the United States during the fourth quarter of 2015, scaled up our manufacturing process for the Sequel Systems and the new SMRT Cells during 2016 and intend to continue to develop and refine our manufacturing processes for increased volume in 2017.

Agreement with Roche

In September 2013, we entered into a Development, Commercialization and License Agreement (the "Roche Agreement") with Roche, pursuant to which we accounted for, and recognized as revenue, the up-front payment received thereunder using the proportional performance method over the periods in which the delivery of elements pursuant to the Roche Agreement occurs. We recognized revenue under the Roche

Agreement using a straight-line convention over the service periods of the deliverables as this method approximated our performance of services pursuant to the Roche Agreement. Out of the $35.0 million upfront cash payment received, quarterly amortization of $1.7 million was recognized as contractual revenue from the fourth quarter of 2013 to the fourth quarter of 2014. Beginning in the three-month period ended March 31, 2015, we revised the estimated development period related to our contractual revenue amortization based on increasing certainty of the development time on a prospective approach and quarterly amortization of $3.6 million was recognized as contractual revenue for each of the four quarters of 2015 and for each of the first three quarters of 2016. As of September 30, 2016, the total deferred contractual revenue balance was $1.3 million, relating to the amount allocated to the deliverable of our participation on the joint steering committee. In December 2016, we received notice from Roche that Roche had elected to terminate the Roche Agreement for convenience. The termination will become effective February 10, 2017, which is 60 days after the date of the notice in accordance with the terms of the Roche Agreement. Upon such termination, no further participation on the joint steering committee is required; as such, we recognized the entire remaining unamortized deferred revenue of $1.3 million as contractual revenue in the fourth quarter of 2016. As a result of Roche's termination of the Roche Agreement, it may be more difficult for us to successfully market, sell and commercialize our products into the markets that Roche would have addressed under the Roche Agreement.

Further, the Roche Agreement provided for additional payments totaling $40.0 million upon the achievement of certain development milestones, all of which have previously been received and recognized as revenue. Consideration from development milestones is recognized in the period in which a milestone is achieved only if the milestone is considered substantive in its entirety. We achieved the first development milestone under the Roche Agreement and recognized the related $10.0 million as contractual revenue during the year ended December 31, 2014. We achieved the second and the third (final) development milestones under the Roche Agreement and recognized the related $10.0 million and $20.0 million as contractual revenue during the three-month periods ended June 30, 2015 and December 31, 2015, respectively. There are no other milestones remaining to be achieved.

Cash Position

Cash, cash equivalents and investments, excluding restricted cash, at December 31, 2016 totaled $72.0 million, compared to $82.3 million at December 31, 2015. During 2016, we also received $58.2 million, net, through the sale of common stock under our "at-the-market" offering. We plan to raise additional capital in the future. To the extent we raise additional funds through the issuance of equity, such issuance will result in dilution to our stockholders. Our cash position is dependent on our revenue, as well as any additional funds raised.

Results of Operations

Comparison of the Years Ended December 31, 2016 and 2015

	Year Ended December 31,			
	2016	2015	$ Change	% Change
	(in thousands, except percentages)			
Revenue:				
Product revenue	$ 64,609	$ 37,502	$ 27,107	72%
Service and other revenue	13,971	10,896	3,075	28%
Contractual revenue	12,134	44,384	(32,250)	(73%)
Total revenue	90,714	92,782	(2,068)	(2%)
Cost of Revenue:				
Cost of product revenue	34,512	30,704	3,808	12%
Cost of service and other revenue	12,042	8,628	3,414	40%
Total cost of revenue	46,554	39,332	7,222	18%
Gross profit	44,160	53,450	(9,290)	(17%)
Operating Expense:				
Research and development	67,617	60,440	7,177	12%
Sales, general and administrative	47,787	45,187	2,600	6%
Gain on lease amendments	—	(23,043)		
Total operating expense	115,404	82,584	32,820	40%
Operating loss	(71,244)	(29,134)	(42,110)	(145%)
Interest expense	(3,234)	(2,926)	(308)	(11%)
Other income (expense), net	103	364	(261)	(72%)
Net loss	$ (74,375)	$ (31,696)	$ (42,679)	(135%)

Revenue

	Year Ended December 31,			
	2016	2015	$ Change	% Change
Revenue:	(in thousands, except percentages)			
Instrument revenue	$ 40,956	$ 18,728	$ 22,228	119%
Consumable revenue	23,653	18,774	4,879	26%
Total product revenue	64,609	37,502	27,107	72%
Service and other revenue	13,971	10,896	3,075	28%
Contractual revenue	12,134	44,384	(32,250)	(73%)
Total revenue	$ 90,714	$ 92,782	(2,068)	(2%)

Total revenue for the year ended December 31, 2016 was $90.7 million compared to $92.8 million for 2015.

Product revenue for the year ended December 31, 2016 consisted of $41.0 million from sales of instruments and $23.7 million from sales of consumables, for total product revenues of $64.6 million, compared to $18.7 million from sales of instruments and $18.8 million from sales of consumables, for total product revenue of $37.5 million, for the year ended December 31, 2015. The increase in sales of instruments from 2015 to 2016 included the effects of the product transition from the PacBio RS II System to the Sequel System. The increase in consumable sales from 2015 to 2016 was primarily attributable to a larger installed instrument base. We expect product revenue to increase in 2017 compared to 2016 based on an expected increase in system shipments and an expected increase in Sequel System utilization.

Service and other revenue for the year ended December 31, 2016 was $14.0 million compared to service revenue of $10.9 million for the year ended December 31, 2015. The increase in service revenue from 2015 to 2016 was primarily attributable to a larger installed instrument base in 2016.

Contractual revenue for the year ended December 31, 2016 was $12.1 million compared to $44.4 million for 2015. Contractual revenue for 2016 included amortization of $3.6 million of the upfront Roche payment for each of the first three quarters of 2016, plus amortization of $1.3 million for the fourth quarter of 2016. As of December 31, 2016, the upfront Roche payment of $35.0 million has been fully recognized. Contractual revenue for 2015 included amortization of $3.6 million of the upfront Roche payment for each of the four quarters of 2015, plus $30.0 million of payments associated with development milestones under the Roche Agreement. We do not expect any contractual revenue for 2017.

Gross Profit

Gross profit for the year ended December 31, 2016 totaled $44.2 million, resulting in a gross margin of 48.7%, compared to a $53.5 million gross profit for the year ended December 31, 2015 and a gross margin of 57.6%. The gross profit and margin for the year ended December 31, 2015 included $30.0 million of milestone revenue from the Roche Agreement at a 100% margin. Excluding this milestone revenue, gross profit and gross margin for the year ended December 31, 2016 increased significantly over 2015 primarily as a result of the higher margin sales of the Sequel System, which was launched in the fourth quarter of 2015.

Cost of product revenue increased to $34.5 million for the year ended December 31, 2016, compared to cost of product revenue of $30.7 million for 2015. The increase in cost of product revenue was primarily driven by the growth of instrument and consumable shipments in 2016 compared to 2015.

Cost of service and other revenue for the year ended December 31, 2016 increased to $12.0 million compared to $8.6 million for the year ended December 31, 2015. The cost of service and other revenue increased in line with the growth in revenue but was partially offset by leveraging existing infrastructure.

Gross margin for 2017 is expected to be lower than 2016, as we have no scheduled contractual revenue to amortize in 2017.

Research and Development Expense

For the year ended December 31, 2016, research and development expenses increased by $7.2 million, or 11.9%, compared to the year ended December 31, 2015. The increase in research and development expenses was primarily attributed to an increase of $6.9 million in compensation related expenses resulting from increased headcount and higher stock-based compensation expenses and an increase of $1.4 million in product development costs related to the launch of the Sequel System, partially offset by a decrease of $1.0 million in professional fees. Research and development expenses included stock-based compensation expenses of $8.3 million and $5.2 million for the years ended December 31, 2016 and 2015, respectively.

We expect our total research and development expenses to increase in 2017 compared to 2016.

Sales, General and Administrative Expense

For the year ended December 31, 2016, sales, general and administrative expenses increased by $2.6 million, or 5.8%, compared to the year ended December 31, 2015. The increase in sales, general and administrative expenses was primarily attributed to an increase of $3.8 million in compensation related expenses resulting from increased headcount and higher stock-based compensation expenses, partially offset by a decrease of $1.1 million in facility expenses due to the rent abatements in 2016. Sales, general and administrative expenses included stock-based compensation expenses of $9.2 million and $7.3 million for the years ended December 31, 2016 and 2015, respectively.

We expect our sales, general and administrative expenses to increase in 2017 compared to 2016.

Interest Expense

Interest expense for the year ended December 31, 2016 remained flat compared to 2015. Interest expense related primarily to the debt facility that we entered into in February 2013.

Liquidity and Capital Resources

Liquidity

Since our inception, we have financed our operations primarily through product sales, issuance of common stock and convertible preferred stock, in addition to our debt facility and payments from Roche pursuant to the terms of the Roche Agreement. Cash, cash equivalents and investments, excluding restricted cash, at December 31, 2016 totaled $72.0 million, compared to $82.3 million at December 31, 2015.

We believe that our existing cash, cash equivalents and investments will be sufficient to fund our projected operating requirements for at least 12 months; however, we plan to raise additional capital in the future. These expectations are based on our current operating and financing plans which are subject to change. Factors that may affect our capital needs include, but are not limited to, slower than expected adoption of our products resulting in lower sales of our products and services; future acquisitions; our ability to obtain new collaboration agreements and maintain customer arrangements; the progress of our research and development programs; initiation or expansion of research programs and collaborations; the costs involved in preparing, filing, prosecuting, defending and enforcing intellectual property rights; the costs of being a public company; the purchase of patent licenses; the costs associated with the ongoing transition to our new facilities in Menlo Park, California; regulatory costs; and other factors.

To the extent 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. There can be no assurance that such funds will be available on favorable terms, or at all. If adequate funds are not available, we may be required to curtail operations significantly or to obtain funds by entering into collaboration agreements on unattractive terms. Our inability to raise capital could have a material adverse effect on our business, financial condition and results of operations.

The following table summarizes our cash flow activities for the periods indicated:

	Year Ended December 31,		
(in thousands)	**2016**	**2015**	**2014**
Net cash provided by (used in):			
Operating activities	$ (67,929)	$ (47,889)	$ (51,468)
Investing activities	(14,864)	8,606	19,564
Financing activities	65,929	36,463	41,991

Operating Activities

Our primary uses of cash in operating activities are for the development of ongoing product enhancements and future products, manufacturing, and support functions related to our sales, general and administrative activities. The net cash used for the years ended December 31, 2016, 2015 and 2014 primarily reflected the net loss for those periods, partially offset by non-cash operating expenses including depreciation and stock-based compensation, as well as changes in working capital.

Cash used in operating activities of $67.9 million in 2016 reflected a net loss of $74.4 million, adjusted for non-cash items such as stock-based compensation of $19.6 million, depreciation and amortization of $3.9 million and amortization of debt discount and financing costs of $1.2 million. Additionally, the change in net operating assets and liabilities was attributed to a reduction in deferred contractual revenue of $12.1 million, an increase in inventory of $6.2 million and an increase of accounts receivable of $6.2 million, partially offset by an increase of $4.5 million of accounts payable and accrued expenses due primarily to the timing of payments. The change in inventory also reflects a transfer of $1.3 million from inventory to fixed assets relating to our instruments.

Cash used in operating activities of $47.9 million in 2015 reflected a net loss of $31.7 million, adjusted for non-cash items such as stock-based compensation of $13.8 million, depreciation and amortization of $3.7 million, the non-cash portion relating to the gain on lease amendments of $3.0 million, and amortization of debt discount and financing costs of $1.0 million. Additionally, the change in net operating assets and liabilities was attributed to an increase of prepaid expenses and other assets of $17.9 million, of which a $15.0 million increase related to the future landlord payments associated with the Lease Amendment Agreement that we entered into in 2015 for our prior headquarters, a reduction in deferred contractual revenue of $14.4 million and a decrease in inventory of $2.5 million, offset by an increase of $5.0 million of accounts payable and accrued expenses due primarily to the timing of payments. The change in inventory also reflects a transfer of $2.8 million from inventory to fixed assets relating to leased PacBio RS II instruments.

Cash used in operating activities of $51.5 million in 2014 reflected a net loss of $66.2 million, partially offset by non-cash, stock-based compensation of $9.9 million and depreciation and amortization of $4.2 million. The change in net operating assets and liabilities was primarily due to an increase of $3.9 million in accounts payable and an increase of $3.5 million in accrued expenses, partially offset by a decrease of $6.8 million in deferred contractual revenue during 2014.

Investing Activities

Our investing activities consist primarily of capital expenditures and investment purchases and maturities.

In 2016, net cash used in investing activities was $14.9 million, comprised of net purchase of investments of $6.7 million and net purchase of property and equipment of $8.2 million.

In 2015, net cash provided by investing activities was $8.6 million, comprised of $16.1 million in net maturities and sales of investments, partially offset by $3.0 million in net purchases of property and equipment, and $4.5 million in long-term restricted cash related to a letter of credit established in October 2015 associated with the lease agreement for our current headquarters.

In 2014, net cash provided by investing activities was $19.6 million, comprised of $21.2 million in net maturities of investments, partially offset by $1.6 million in purchases of property and equipment.

Financing Activities

In 2016, cash provided by financing activities was $65.9 million, comprised of net proceeds of $58.2 million from our common stock “at-the-market” offering program and $7.7 million from the issuance of common stock through our equity compensation plans.

In 2015, cash provided by financing activities was $36.5 million, comprised of net proceeds of $29.1 million from our common stock “at-the-market” offering program and $7.4 million from the issuance of common stock through our equity compensation plans.

In 2014, cash provided by financing activities was $42.0 million, comprised of net proceeds of $38.0 million from our common stock “at-the-market” offering program and $4.0 million from the issuance of common stock through our equity compensation plans.

Capital Resources

Common Stock “At-the-Market” Offering

During April 2012, we filed a shelf registration statement on Form S-3 with the SEC pursuant to which we could, from time to time, sell up to an aggregate of $150.0 million of our common stock, preferred stock, depository shares, warrants, units or debt securities. On May 1, 2012, the registration statement was declared effective by the SEC, which allowed us to access the capital markets for three years following the effective date.

On October 5, 2012, we entered into a sales agreement pursuant to which we sold shares of our common stock having an aggregate offering price of approximately $30.0 million through an “at-the-market” offering.

On November 8, 2013, we amended the sales agreement to increase the shares of our common stock available for sale pursuant to the sales agreement, and pursuant to such amendment, sold additional shares of our common stock for an aggregate offering price of approximately $30.0 million.

In November 2014, we filed a shelf registration statement on Form S-3 with the SEC pursuant to which we may, from time to time, sell up to an aggregate of $150.0 million of our common stock, preferred stock, depositary shares, warrants, units or debt securities. On November 21, 2014, the registration statement was declared effective by the SEC, which would allow us to access the capital markets for three years following the effective date.

On February 3, 2015, we amended the sales agreement again in order to further increase the shares of our common stock available for sale pursuant to the sales agreement, and pursuant to such amendment, sold additional shares of our common stock for an aggregate offering price of approximately $30.0 million.

On February 3, 2016, we filed a prospectus supplement pursuant to which we could offer and sell, from time to time, additional shares of our common stock having an aggregate offering price of up to $30.0 million under the sales agreement. Such aggregate offering price of shares of our common stock was in addition to the shares sold under the original sales agreement, dated October 5, 2012, the first amendment to the sales agreement, dated November 8, 2013, and the second amendment to the sales agreement, dated February 3, 2015. Pursuant to the prospectus supplement, we sold additional shares of our common stock for an aggregate offering price of approximately $30.0 million.

On May 18, 2016, we filed a prospectus supplement pursuant to which we could offer and sell, from time to time, additional shares of our common stock having an aggregate offering price of up to $30.0 million under the sales agreement. Pursuant to such prospectus supplement, we sold additional shares of our common stock for an aggregate offering price of approximately $30.0 million.

We pay a commission equal to 3% of the gross proceeds from the sale of shares of our common stock under the sales agreement. We are not obligated to sell shares of our common stock under the sales agreement.

In February 2017, we intend to file an additional prospectus supplement pursuant to which we may offer and sell, from time to time, additional shares of our common stock having an aggregate offering price of up to $60.0 million under the sales agreement.

We may need to raise additional capital in the future through the sale of equity or convertible debt securities, including future “at-the-market” offerings.

Debt Facility Agreement

Under the terms of our February 2013 debt agreement with Deerfield (the "Facility Agreement"), we received $20.5 million and issued promissory notes in the aggregate principal amount of $20.5 million (the "Notes"). The Notes bear simple interest at a rate of 8.75% per annum, payable quarterly in arrears commencing on April 1, 2013 and on the first business day of each January, April, July and October thereafter. The Facility Agreement has a maximum term of seven years. We received net proceeds of $20.0 million, representing $20.5 million of gross proceeds, less a $500,000 facility fee, before deducting other expenses of the transaction.

The Facility Agreement also contains various representations and warranties, and affirmative and negative covenants, customary for financings of this type, including restrictions on our ability to incur additional indebtedness or liens on our assets, except as permitted under the Facility Agreement. In addition, the Facility Agreement requires us to maintain consolidated cash and cash equivalents on the last day of each calendar quarter of not less than $2.0 million. As security for our repayment of our obligations under the Facility Agreement, we granted the lenders a security interest in substantially all of our property and interests in property.

Subject to certain exceptions set forth in the Facility Agreement, holders representing a majority of the aggregate principal amount of the outstanding Notes issued pursuant to the Facility Agreement may elect to receive 25% of the net proceeds from any financing that includes an equity component. To the extent we raise additional capital in the future through the sale of common stock, including without limitation, sales of common stock pursuant to an "at-the-market" offering program, we may be obligated, at the election of the holders of the Notes, to pay 25% of the net proceeds from any such financing activities as partial payment of the Notes.

Contractual Obligations, Commitments and Contingencies

Leases

In December 2009, we entered into a lease agreement for a manufacturing and office facility in Menlo Park. In order for the facility to meet our needs and operating requirements, substantial tenant improvements, including improvements to the structural elements and principal operating systems of the facility, were necessary. The lessor provided a tenant improvement allowance of $1.8 million to apply towards the necessary improvements and we remained obligated for additional amounts over the afforded allowance. Due to our involvement in and the nature of the renovations made to the facility and our obligations to fund the costs of renovations exceeding the incentives afforded to us, we account for the facility as if we are the owner. Accordingly, we recorded $3.0 million of building and leasehold improvement assets, reflecting the $1.2 million fair value of the facility prior to commencing renovations and the $1.8 million of landlord incentives within property and equipment, net and a corresponding liability recorded to facility financing obligation.

As a result of the lease amendment agreement described below, future rent expense associated with our existing Menlo Park facility leases was reduced to zero. The remaining long-term facility financing obligations associated with these leases, presented as "Other liabilities, non-current" on the consolidated balance sheets at December 31, 2016 and December 31, 2015, were $1.7 million and $1.4 million, respectively.

Lease Amendment Agreement

On July 23, 2015, we entered into a Lease Amendment Agreement (the "Lease Amendment Agreement") with Peninsula Innovation Partners, LLC (the "Existing Landlord"), which amends the terms and conditions of certain of our existing Menlo Park facility real property leases. The Lease Amendment Agreement provides for, among other things, amendments of the term for certain of the leases with the Existing Landlord, the termination of all renewal, expansion and extension rights contained in any of the existing leases with the Existing Landlord (including our options to extend the terms for certain of the existing leases for two consecutive five-year periods), as well as rent abatement for a specified period of time. As consideration for our agreement to amend the existing leases pursuant to the Lease Amendment Agreement, and subject to the terms and conditions contained therein, we became eligible to receive up to four payments of $5.0 million each from the Existing Landlord over time (the "Landlord Payments"), and rent abatement for the remainder of the lease. In the event that we breach any of the leases and fail to cure such breach within the time permitted, the Existing Landlord would have no obligation to make the final $5.0 million payment. On September 1, 2015, the permit process related to an architectural approval and a change of use permit with respect to our new premises at 1305 O'Brien Drive (formerly 1315 O'Brien Drive), Menlo Park, California (the "O'Brien Premises") was completed, which satisfied the contingencies under the Lease Amendment Agreement. As a result, we recorded $23.0 million in "Gain on lease amendments" in the consolidated statements of operations and comprehensive loss for the three-month period ended September 30, 2015, reflecting that our rent payments were reduced to zero for the remaining term of our existing Menlo Park facility real property leases, and the aggregate of $20.0 million in Landlord Payments became receivable and any associated financing obligation was revalued. Of the $20.0 million remaining Landlord Payments, the first $5.0 million Landlord Payment was received in September 2015, the second $5.0 million Landlord Payment was received in February 2016 and the third $5.0 million Landlord Payment was received in August 2016.

In June 2016, we entered into a Second Lease Amendment Agreement with the Existing Landlord that modified the payment schedule for the final $5.0 million. At December 31, 2016, the final $5.0 million was recorded in "Prepaid Expenses and Other Current Assets" in the consolidated balance sheets. We do not believe that there are any remaining performance obligations relating to the remaining Landlord Payments. In January 2017, we entered into a Third Lease Amendment Agreement with the Existing Landlord that increased the amount of the payments receivable from the Existing Landlord by $65,000.

O'Brien Lease Agreement

On July 22, 2015, we entered into a new lease agreement (the "O'Brien Lease") with respect to the O'Brien Premises. The term of the O'Brien Lease is one hundred thirty-two (132) months, commencing on the date that is the later of April 15, 2016 or the date on which the O'Brien Premises landlord has substantially completed certain shell improvements and tenant improvements. In December 2016, we entered

into an amendment to the O'Brien Lease which defined the commencement date of the lease to be October 25, 2016, notwithstanding that such substantial completion date has not yet occurred. We did not have control of the building until after December 31, 2016. Base monthly rent will be abated for the first six (6) months of the lease term and thereafter will be $540,000 per month during the first year of the lease term, with specified annual increases thereafter until reaching $711,000 per month during the last twelve (12) months of the lease term. We were required to pay $2,160,000 in prepaid rent which will be applied to the monthly rent installments due for the first to fourth months after the rent abatement period. We were required to establish a deposit of $4.5 million in the form of a letter of credit in October 2015; and, as such, $4.5 million was recorded in "Long-term restricted cash" in the consolidated balance sheet as of both December 31, 2016 and December 31, 2015. The landlord is obligated to construct certain shell improvements at the landlord's cost and expense and provide us with improvement allowances in the amount of $12.6 million.

Under the O'Brien Lease, we expect to pay approximately $80.0 million in rent and $24.0 million in operating expenses over the expected lease term. In addition to the lease payments, we are also required to reimburse the landlord for certain improvement costs in excess of the tenant improvement allowances provided. These improvement costs, along with the costs associated with the anticipated move to the O'Brien Premises, are expected to be substantial in nature. These future expenditures are expected to be partially offset by the $5.065 million of future Landlord Payments from our Existing Landlord as described above.

The following table provides summary information concerning our future contractual obligations as of December 31, 2016.

	Payments due by period (in thousands)						
	Total	2017	2018	2019	2020	2021	After
Operating lease obligations (1)	$ 79,666	$ 4,749	$ 6,949	$ 6,930	$ 7,056	$ 7,272	$ 46,710
Debt (2)	25,837	1,794	5,375	2,816	15,852	—	—
Purchase commitments and obligations	18,041	18,041	—	—	—	—	—
Total contractual obligations	$ 123,544	$ 24,584	$ 12,324	$ 9,746	$ 22,908	$ 7,272	$ 46,710

(1) Maintenance, insurance, taxes and contingent rent obligations are excluded.

(2) Under the terms of the Facility Agreement and the Notes, we received $20.5 million in funding. The amounts in the table above include interest and principal repayments on the debt.

Purchase Commitments and Obligations

These amounts include an estimate of all open purchase orders and contractual obligations in the ordinary course of business, including commitments with contract manufacturers and suppliers, for which we have not received the goods or services. A majority of these purchase obligations are due within a year. Although open purchase orders are considered enforceable and legally binding, the terms generally allow us the option to cancel, reschedule, and adjust our requirements based on our business needs prior to the delivery of goods or performance of services.

The table above reflects only payment obligations that are fixed and determinable. Future milestone payments and royalties under our license agreements are not included in the table above because we cannot, at this time, determine when or if the events triggering any such payment obligations will occur or the amounts that will become potentially payable.

License Agreements

Payments related to licensing and other arrangements not included in the contractual obligations table include amounts related to cancelable license agreements with third parties for certain patent rights and technology. Under the terms of these agreements, we may be obligated to pay royalties based on revenue from the sales of licensed products, or minimum royalties, whichever is greater, and license maintenance fees. The future license maintenance fees and minimum royalty payments under the license agreements are not deemed to be material.

Legal Proceedings

On November 2, 2016, we filed a complaint against Oxford Nanopore Technologies Ltd., Oxford Nanopore Technologies, Inc. and Metrichor, Ltd. (together, "ONT") with the U.S. International Trade Commission ("USITC") for patent infringement. On December 5, 2017, the USITC provided notice that an investigation had been instituted based on the complaint. We are seeking exclusionary relief with respect to several ONT products, including ONT's MinION and PromethION devices. The complaint is based on our U.S. Patent No. 9,404,146, entitled "Compositions and methods for nucleic acid sequencing" which covers novel methods for sequencing single nucleic acid molecules using linked double-stranded nucleic acid templates, providing improved sequencing accuracy. We have notified the Commission of our intention to add a second patent in the same patent family, U.S. Patent No. 9,542,527, which was granted on January 10, 2017, to the investigation. We are seeking, among other things, an exclusion order permanently barring entry of infringing ONT products into the United States, and a cease and desist order preventing ONT from advertising and selling infringing products in the United States.

From time to time, we may also be involved in a variety of other claims, lawsuits, investigations and proceedings relating to securities laws, product liability, patent infringement, contract disputes, employment and other matters that arise in the normal course of our business. In

addition, third parties may, from time to time, assert claims against us in the form of letters and other communications. We record a provision for contingent losses when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated. We currently do not believe that the ultimate outcome of any of the matters described above is probable or reasonably estimable, or that these matters will have a material adverse effect on our business; however, the results of litigation and claims are inherently unpredictable. Regardless of the outcome, litigation can have an adverse impact on us because of litigation and settlement costs, diversion of management resources and other factors.

BUSINESS

Overview

We design, develop and manufacture sequencing systems to help scientists resolve genetically complex problems. Based on our novel Single Molecule, Real-Time (SMRT®) Sequencing technology, our products enable: *de novo* genome assembly to finish genomes in order to more fully identify, annotate and decipher genomic structures; full-length transcript analysis to improve annotations in reference genomes, characterize alternatively spliced isoforms in important gene families, and find novel genes; targeted sequencing to more comprehensively characterize genetic variations; and real-time kinetic information for epigenome characterization. Our technology provides high accuracy, ultra-long reads, uniform coverage, and is the only DNA sequencing technology that provides the ability to simultaneously detect epigenetic changes. PacBio® sequencing systems, including consumables and software, provide a simple, fast, end-to-end workflow for SMRT Sequencing.

Our customers and our scientific collaborators have published numerous peer-reviewed articles in journals including Nature, Science, Cell, PNAS and The New England Journal of Medicine highlighting the power and applications of SMRT sequencing in projects such as finishing genomes, structural variation discovery, isoform transcriptome characterization, rare mutation discovery and the identification of chemical modifications of DNA related to virulence and pathogenicity. Our research and development efforts are focused on developing new products and further improving our existing products, including continuing chemistry and sample preparation improvements to increase throughput and expand our supported applications. By providing access to genetic information that was previously inaccessible, we enable scientists to confidently increase their understanding of biological systems.

Pacific Biosciences of California, Inc., formerly Nanofluidics, Inc., was incorporated in the State of Delaware in 2000. Our executive offices are located at 1305 O'Brien Drive, Menlo Park, California 94025, and our telephone number is (650) 521-8000.

The Underlying Science

Genetic inheritance in living systems is conveyed through a naturally occurring information storage system known as deoxyribonucleic acid, or DNA. DNA stores information in linear chains of the chemical bases adenine, cytosine, guanine and thymine, represented by the symbols A, C, G and T respectively. Inside living cells, these chains usually exist in pairs bound together in a double helix by complementary bases, with A of one strand always binding to a T of the other strand and C always binding to G.

In humans, there are approximately three billion DNA base-pairs in the molecular blueprint of life, called the genome. These three billion bases are divided into 23 chromosomes ranging in size from 50 million to 250 million bases. Normally, there are two complete copies of the genome contained in each cell, one of maternal origin and the other of paternal origin. When cells divide, the genomes are replicated by an enzyme called DNA polymerase, which visits each base in the sequence, creating a complementary copy of each chromosome using building blocks called nucleotides. Contained within these chromosomes are approximately 23,000 smaller regions, called genes, each one containing the recipe for a protein or group of related proteins. The natural process of protein production takes place in steps. In a simplified model, the first step is transcription, a process in which an enzyme called RNA polymerase uses DNA as a template to synthesize new strands of messenger RNA, or mRNA. The mRNAs are then translated into proteins by ribosomes. The resulting proteins go on to play crucial roles in cellular structure and function and thus the operation of biological systems.

Numerous scientific approaches have evolved to adapt to the emerging awareness of the magnitude of complexity embedded in biological systems. The field of genomics developed to study the interactions among components in the genome and the massive quantities of associated data. Subsequently, proteomics, transcriptomics and a number of other related fields emerged.

Advances in biology over the next decade are expected to be shaped by a more detailed understanding of the fundamental complexity of biological systems. These systems vary among individuals in previously unrecognized ways and are influenced by factors including time, molecular interactions, and cell type.

Importantly for the future of genomics, the first few whole-genome sequencing studies of disease have shown that rare mutations play a critical role in human disease. These mutations would not have been detected in earlier studies because too few people, or perhaps only one person, carry the specific mutation. In addition, it is now understood that structural changes to the genome in which whole sections are deleted, inverted, copied or moved may be responsible for a significant fraction of variation among individuals. The scope of these structural changes challenges the very idea of a reference genome.

Recent discoveries have highlighted additional complexities in the building blocks of DNA and RNA, including the presence of modified bases. It has long been known that in humans and many other organisms, the cytosine bases can be chemically modified through the addition of a methyl group in a process called methylation, resulting in modified bases such as 5-methylcytosine (5-mC) and N^4-methylcytosine (4-mC). These chemical modifications have been shown to play a role in embryonic development, have important impacts on diseases such as cancer

and can even affect the characteristics of offspring for multiple generations. More recently, it has been discovered that other modified bases, such as 5-hydroxymethylcytosine, 8-oxoguanine and many others, play important physiological roles. For example, in bacteria, N^6-methyladenine (6-mA) has been shown to play an important role in pathogenicity.

Another source of complexity derives from the processing of RNA molecules after being transcribed from the genome. The majority of all genes code for different forms of a protein that can be made depending on the structure of the RNA molecule, referred to as splice variants. A detailed understanding of both the expression pattern and regulation of these variants is believed to play an important role in a number of critical biological processes.

Recent advances in our understanding of biological complexity have highlighted the need for advanced tools such as the PacBio® RS II System and the Sequel™ System to study DNA, RNA and proteins. In the field of DNA sequencing, incremental technological advances have provided novel insights into the structure and function of the genome. Despite these advances, scientists have not been able to fully characterize the human genome and the genomes of other living organisms because of inherent limitations in these tools.

Evolution of Sequencing

In order to understand the limitations of current DNA sequencing technologies, it is important to understand the sequencing process. This consists of three phases: sample preparation, physical sequencing, and analysis. The first step of sample preparation is to either break the target genome into multiple small fragments or, depending on the amount of sample DNA available, amplify the target region using a variety of molecular methods. In the physical sequencing phase, the individual bases in each fragment are identified in order, creating individual reads. The number of individual bases identified contiguously is defined as read length. In the analysis phase, bioinformatics software is used to align overlapping reads, which allows the original genome to be assembled into contiguous sequence. The longer the read length, the easier it is to assemble the genome.

Sanger Sequencing

The first automated sequencing methodology, often referred to as “Sanger sequencing,” was developed by Frederick Sanger in 1977. With this technology, during sample preparation, scientists first make different sized fragments of DNA each starting from the same location. Each fragment ends with a particular base that is labeled with one of four fluorescent dyes corresponding to that particular base. Then all of the fragments are distributed in order of their length by driving them through a gel. Information regarding the last base is used to determine the original sequence. Under standard conditions, this method results in a read length that is approximately 700 bases on average, but may be extended to 1,000 bases. These are relatively long read lengths compared with many next-generation sequencing methods. However, Sanger sequencing is limited by the small amounts of data that can be processed per unit of time, referred to as throughput.

Short-read Sequencing

Several commercial DNA sequencing tools emerged in 2005 in response to the low throughput of Sanger sequencing. Now commonly referred to as “short-read sequencing”, these methods achieve much higher throughput by sequencing a large number of DNA molecules in parallel, but with the tradeoff of shorter read lengths.

In most short-read sequencing methodologies, tens of thousands of identical strands are anchored to a given location to be read in a process consisting of successive flushing and scanning operations. The “flush and scan” sequencing process involves sequentially flushing in reagents, such as labeled nucleotides, incorporating nucleotides into the DNA strands, stopping the incorporation reaction, washing out the excess reagent, scanning to identify the incorporated base and finally treating that base so that the strand is ready for the next “flush and scan” cycle. This cycle is repeated until the reaction is no longer viable.

Due to the large number of flushing, scanning and washing cycles required, the time to result for short-read sequencing methods can be longer, sometimes taking days. This repetitive process also limits the average read length produced by most of these systems under standard sequencing conditions to approximately 35 to 400 bases.

The short-read sequencing technologies require a large number of DNA molecules during the sequencing process. To generate enough DNA molecules, a copying method called PCR amplification is required during sample preparation. This amplification process can introduce errors known as amplification bias. The effect of this bias is that resulting copies are not uniformly representative of the original template DNA. In cases where the original template DNA contains regions of relatively high G-C content or relatively high A-T content, the PCR amplification process tends to under-represent these regions. As a result, these regions, which may contain entire genes, can be completely missed.

In summary, while short-read sequencing methods can offer very high throughput and low cost per identified base, their disadvantages can include limited read length, variation in sequence coverage with regard to representation bias and accuracy, dependence on amplification, long time to result, and/or a need for many samples to justify machine operation.

The PacBio Solution — Single Molecule, Real-Time Technology

We have developed our SMRT technology, which enables single molecule, real-time detection of biological processes, to address many of the limitations of previous sequencing technologies. By providing long read lengths, elimination of the dependence on amplification during sample preparation (which can result in amplification bias), very high consensus accuracy, and the ability to detect DNA base modifications, the PacBio RS II System and the Sequel System provide more comprehensive and higher quality information of DNA and RNA sequence as well as epigenetic regulation and DNA damage.

Pacific Biosciences' SMRT Technology

SMRT technology enables the observation of DNA synthesis as it occurs in real time by harnessing the natural process of DNA replication, which in nature is a highly efficient and accurate process actuated by the DNA polymerase. The DNA polymerase attaches itself to a strand of DNA to be replicated, examines the individual base at the point it is attached, and then determines which of four building blocks, or nucleotides, is required to complement that individual base. After determining which nucleotide is required, the polymerase incorporates that nucleotide into the growing strand being produced. After incorporation, the enzyme advances to the next base to be replicated and the process is repeated.

To overcome the challenges inherent in real-time observation of the natural activity of the DNA polymerase, an enzyme measuring approximately 15 nanometers (nm) in diameter, we offer three key innovations:

- The SMRT Cell
- Phospholinked nucleotides
- The PacBio RS II and Sequel instruments

The SMRT Cell

One of the fundamental challenges with observing a single DNA polymerase molecule working in real time is the ability to detect the incorporation of a single nucleotide, taken from a large pool of potential nucleotides, during DNA synthesis. To resolve this problem, we utilize our nanoscale innovation, the zero-mode waveguide, or ZMW.

The ZMWs in our SMRT Cells consist of holes in an opaque layer, measuring only tens of nanometers in diameter forming nanoscale wells. The small size of the ZMW causes the intensity of visible laser light, which has a wavelength of approximately 600nm, to decay exponentially in the ZMW. Therefore, laser light shined into the ZMW from below is blocked from reaching the sequencing solution above the ZMW, providing selective illumination of only the bottom portion of the nanoscale well. DNA polymerases are anchored to the bottom of the glass surface of the nanoscale wells using proprietary techniques. Nucleotides, each type labeled with a different colored fluorophore, are then flooded above an array of ZMWs at the required concentration. When the labeled nucleotides diffuse into the bottom portion of the nanoscale wells, which contain the anchored DNA polymerases, their fluorescence can be monitored. When the correct nucleotide is detected by the polymerase, it is incorporated into the growing DNA strand in a process that takes milliseconds in contrast to simple diffusion which takes microseconds. This difference in time results in higher signal intensity for incorporated versus unincorporated nucleotides, which creates a high signal-to-noise ratio. Thus, the ZMW provides the ability to detect a single incorporation event against the background of fluorescently labeled nucleotides at biologically relevant concentrations. Our DNA sequencing is performed on proprietary SMRT Cells, each having an array of ZMWs. The SMRT Cells for the PacBio RS II System each contain approximately 150,000 ZMWs, whereas the SMRT Cells for the Sequel System each contain approximately one million ZMWs. Each ZMW is capable of containing a DNA polymerase molecule bound to a single DNA template. Currently, our immobilization process randomly distributes polymerases into ZMWs across the SMRT Cell, resulting in approximately one-third of the ZMWs having a single template.

Phospholinked Nucleotides

Our proprietary phospholinked nucleotides have a fluorescent dye attached to the phosphate chain of the nucleotide rather than to the base. As a natural step in the synthesis process, the phosphate chain is cleaved when the nucleotide is incorporated into the DNA strand. Thus, upon incorporation of a phospholinked nucleotide, the DNA polymerase naturally frees the dye molecule from the nucleotide when it cleaves the phosphate chain. Upon cleaving, the label quickly diffuses away, leaving a natural piece of DNA without evidence of labeling.

The PacBio RS II and Sequel Instruments

The PacBio RS II and Sequel instruments conduct, monitor, and analyze single molecule biochemical reactions in real time. The instruments use extremely sensitive imaging systems to collect the light pulses emitted by fluorescent reagents allowing the observation of biological processes. Computer algorithms are used to translate the information that is captured by the optics system. Using the recorded information, light pulses are converted into either an A, C, G or T base call with associated quality metrics. Once sequencing is started, the real-time data is delivered to the system's primary analysis pipeline, which outputs base identity and quality values, or QVs. To generate a consensus sequence from the data, an assembly process assembles the different fragments from each ZMW based on common sequences.

SMRT Sequencing Advantages

Sequencing based on our SMRT technology offers the following key benefits:

- *Longer read lengths*

SMRT technology has been demonstrated to produce read lengths that are significantly longer than those of previous sequencing technologies. Long read lengths are necessary to span repetitive regions to efficiently assemble genomes. Long read lengths are an important factor in enabling a comprehensive view of the genome, as they can reveal multiple types of genetic variation such as structural variants.

- *High consensus accuracy*

Users of SMRT technology can achieve very high consensus accuracy due to the attributes of SMRT sequencing, including long read lengths, lack of reliance on amplification during sample preparation (which can result in amplification bias), and lower systematic

bias. Users of short-read sequencing technologies often cannot achieve comparable results due to their shorter read lengths and systematic bias.

- *More uniformity and less systematic error*

The sample preparation step for SMRT sequencing is compatible with but does not require amplification; when amplification is not used during sample preparation, the reads are not subject to amplification bias. Importantly, this allows for uniform identification of all bases present in a DNA sample and uniform sequence coverage. As a result, SMRT sequencing can detect and identify regions and entire genes that may be missed by short-read sequencing technologies.

- *Ability to observe and capture kinetic information*

The ability to observe the activity of a DNA polymerase in real time enables the PacBio RS II and Sequel Systems to collect, measure and assess the dynamics and timing of nucleotides being added to a growing DNA strand, referred to as kinetics. It is well established in the scientific community that chemical modification of DNA such as the addition of a methyl group, known as methylation, can alter the biological activity of the affected nucleotide. The PacBio RS II and Sequel Systems detect changes in kinetics automatically by capturing and recording changes in the duration of, and time period between, each of the fluorescent pulses during a typical sequencing analysis. Integrated software can then translate these kinetic signatures into uniquely characterized modified bases such as 6-mA, 4-mC and 5-mC. Other sequencing systems, which rely on a sample preparation amplification step or are limited by signal resolution, are unable to directly measure this type of kinetic data.

- *Flexibility*

Our sequencing systems have the ability to scale the throughput and cost of sequencing across a range of small to large projects. They can be used with a variety of sample types and can output a range of DNA lengths.

Our Products

We entered the market with our first commercial product, the PacBio *RS* System, during the second quarter of 2011 and launched the higher performance PacBio RS II System during the second quarter of 2013. In September of 2015, we announced the Sequel System, which is based on the same underlying SMRT technology as the PacBio RS II System, but can achieve up to approximately seven times the throughput with newly-designed SMRT Cells. Our sequencing systems provide access to a wide range of applications and are designed for expandable improvements to performance capability and new application capabilities through chemistry and software enhancements without necessitating changes to instrument hardware.

PacBio Systems

The PacBio RS II and Sequel Systems conduct, monitor, and analyze biochemical sequencing reactions. The PacBio RS II and Sequel instruments are integrated units that include high performance optics, automated liquid handling, a touchscreen control interface and computational hardware and software. Each instrument's high performance optics monitor the ZMWs in a SMRT Cell in real time. The automated liquid handling system performs reagent mixing and prepares SMRT Cells. Each instrument's touchscreen control interface is the user's primary control center to design and monitor experiments. The computational hardware and software in each instrument is responsible for processing the sequencing data produced by the SMRT Cells. Both the PacBio RS II System and the Sequel System have been designed to allow for performance improvements to be easily integrated into the systems.

Consumables

Customers must purchase proprietary consumable products to run either the PacBio RS II System or Sequel System. Our consumable products include our proprietary SMRT Cells and reagent kits. One SMRT Cell is consumed per sequencing reaction, and scientists can choose the number of SMRT Cells they use per experiment. For the PacBio RS II instrument, eight SMRT Cells containing approximately 150,000 ZMWs each are individually and hermetically sealed then packaged together into a streamlined 8Pac format. Sequel System customers purchase a similarly packaged, four SMRT Cell format with approximately one million ZMWs each.

We offer several reagent kits, each designed to address a specific step in the workflow. A template preparation kit is used to convert DNA into SMRTbell™ double-stranded DNA library formats and includes typical molecular biology reagents, such as ligase, buffers and exonucleases. Our binding kits include our modified DNA polymerase, and are used to bind SMRTbell libraries to the polymerase in preparation for sequencing. Our sequencing kits contain reagents required for on-instrument, real-time sequencing, including the phospholinked nucleotides.

Product Enhancements

Since the introduction of our products in 2011, we have continued to significantly enhance the performance of PacBio sequencing systems through a combination of sample preparation protocol enhancements, software releases, and new sequencing reagent chemistries. By providing an increasing number of longer reads per instrument run, the new chemistries have enabled users to assemble more genomes to a high quality. We have continually improved our software to expand the number of supported applications such as large genome assembly, sequencing of transcript isoforms produced from genes, and phasing of haplotypes in large amplicons. During 2017, we plan to further improve our existing products, including chemistry and sample preparation improvements to increase throughput and expand our supported applications, and to continue to develop new products.

Market for Our Products

Our customers use our products for sequencing genomes and transcriptomes across a wide range of organisms. Initially, customers in research, government and commercial markets used the PacBio *RS* and RS II Systems to generate more complete assemblies of small and medium size genomes, such as bacteria and fungi, and for sequencing targeted regions of larger genomes such as humans and plants. As throughput and read lengths have increased, the complexity and size of genomes being resolved with SMRT sequencing have grown. Scientists now use SMRT sequencing to generate genome assemblies of humans, plants & animals, characterize transcriptomes through full-length isoform sequencing, and phase complex genomic regions like full-length human leukocyte antigen, or HLA, genes. With the introduction of the Sequel System, our higher throughput and lower cost platform for SMRT sequencing, we anticipate increasing both mindshare and market share within research and commercial markets such as human biomedical research, plant and animal sciences, microbiology & infectious disease, and immunogenomics.

There are a number of emerging markets for sequencing-based tests, including molecular diagnostics, which represent significant potential opportunities for our products. The development of these markets is subject to variability driven by ongoing changes in the competitive landscape, evolving regulatory requirements, government funding of research and development activities, and macroeconomic conditions. Introductions of new technologies and products, while positive to the overall development of these markets, may result in greater competition for the limited financial resources available. As we continue to expand into these emerging markets, the development of our business will be impacted by the variability of the factors affecting the growth of these markets.

Pacific Biosciences' Strategy

Key elements of our strategy include:

· ***Offer differentiated products based on our proprietary SMRT technology***

Our SMRT technology provides a window into biological processes that has not previously been available. The combination of our products' and underlying SMRT technology's ability to deliver long read lengths, high consensus accuracy, low bias, and kinetic information affords the scientific community a new tool to conduct research not possible with other sequencing technologies.

· ***Enhance product performance and introduce new products to increase market share.***

The design of our sequencing systems allows for significant performance improvements. Our flexible platforms are designed to generate a recurring revenue stream through the sale of proprietary SMRT Cells and reagent kits. With the introduction of the Sequel System, our higher throughput and lower cost platform for SMRT sequencing, we anticipate increasing both market recognition and market share within the markets for our products. We plan to introduce additional product enhancements over time to further reduce DNA sequencing project costs and time to result while expanding application solutions.

·***Create a global community of users to enhance informatics capabilities, develop sample preparation solutions, and drive adoption of our products in new application and market areas.***

We work closely with our customers and collaborators to develop new applications and demonstrate SMRT sequencing capabilities on scientifically relevant projects. We partner with members of the informatics community to develop and define standards for working with single molecule, real-time sequence data. We maintain the PacBio DevNet site, a website on which we make available various software tools and information about our SMRT sequencing technology to support academic informatics developers, scientists and independent software vendors interested in creating tools to work with SMRT sequencing data. This gives the user flexibility to perform further analysis of the sequencing data through third-party software or share data with collaborators. To help maximize the flexibility and functionality for users, our secondary analysis algorithms are made available under open source licenses. We also make available on our main corporate website various methods developed internally and externally for simplifying and enhancing sample preparation protocols.

·***Leverage SMRT technology and community engagement to expand application capabilities and penetrate new markets.***

We plan to leverage our customers' successes with SMRT sequencing to expand the capabilities of our products for applications our customers have identified as high-value based on the differentiating attributes of our technology. Early applications identified by our customers include: whole genome sequencing, targeted sequencing of complex regions, isoform discovery and characterization, resolution of complex populations, and epigenetic analysis. We plan to develop whole product solutions around these applications, making it easier for customers who are not typically early adopters of new technology to take advantage of SMRT sequencing.

In the long term, we believe that our SMRT technology may also be adapted for RNA transcription monitoring, direct RNA sequencing, protein translation and ligand binding. We believe these applications can create substantial new markets for our technology.

Marketing, Sales, Service and Support

We market our products through a direct sales force in North America and Europe and primarily through distribution partners in Asia and parts of the Middle East and Latin America. Our sales strategy involves the use of a combination of sales personnel and field application scientists. The role of our sales personnel is to educate customers on the advantages of SMRT technology and the applications that our technology makes possible. The role of our field application scientists is to provide on-site training and scientific technical support to prospective and existing customers. Our field application scientists are technical experts, often with advanced degrees, and generally have extensive experience in academic research and core sequencing lab experience.

Service for our instruments is performed by field service engineers. These field service engineers are trained by experienced personnel to test, trouble-shoot, and service instruments installed at customer sites.

In addition, we maintain an applications lab team in Menlo Park, California composed of scientific experts who can transfer knowledge from the research and development team to the field application scientists. The applications lab team also runs foundational scientific collaborations and proof of principle studies, which help demonstrate the value of our product offering to prospective customers.

Customers

Our customers include research institutions, commercial laboratories, genome centers, clinical, government and academic institutions, genomics service providers, pharmaceutical companies and agricultural companies. In general, our customers will isolate, prepare and analyze genetic samples using PacBio sequencing systems in their own research labs to address their specific applications and scientific questions. For example, customers in academic research institutions may have bacteria, animal, or human DNA samples isolated from various sources while agricultural biology companies may have DNA samples isolated from different strains of rice, corn or other crops. For the years ended December 31, 2016, 2015 and 2014, excluding contractual revenue, no single end customer accounted for more than 10% of our total revenue.

We believe that the majority of our current customers are early adopters of sequencing technology. By focusing our efforts on high-value applications, and developing whole product solutions around these applications, we seek to drive the adoption of our products across a broader customer base and into numerous large-scale projects. In general, the broader adoption of new technologies by mainstream customers can take a number of years.

We currently sell our products to a number of customers outside the United States, including customers in other areas of North America, Europe, Asia, the Middle East, and Latin America. Roche related contractual revenue has been classified as revenue from the United States. Revenue from customers outside the United States totaled $41.0 million, or 45% of our total revenue during fiscal 2016, compared to $24.9 million, or 27% of our total revenue, during fiscal 2015, and compared to $26.2 million, or 43% of our total revenue, during fiscal 2014.

Backlog

As of December 31, 2016, our instrument backlog was approximately $11.0 million, compared to $16.7 million as of December 31, 2015. We define backlog as purchase orders or signed contracts from our customers which we believe are firm and for which we have not yet recognized revenue. We expect to convert this backlog to revenue during 2017; however, our ability to do so is subject to customers who may seek to cancel or delay their orders even if we are prepared to fulfill them.

Manufacturing

Our principal manufacturing facilities are located at our prior headquarters in Menlo Park, California with part of the facilities also being located at our new headquarters at the O'Brien Premises during the relocation process. We currently perform some of the manufacturing and all of the final integration of our instruments in-house, while outsourcing most sub-assemblies to third-party manufacturers. With respect to the manufacture of SMRT Cells, we subcontract wafer fabrication and processing to semiconductor processing facilities, but conduct critical surface treatment processes internally. In addition, we currently manufacture critical reagents in-house, including our phospholinked nucleotides and our DNA polymerase.

We purchase both custom and off-the-shelf components from a large number of suppliers and subject them to significant quality specifications. We periodically conduct quality audits of most critical suppliers and have established a supplier certification program. We purchase components through purchase orders. Some of the components required in our products are currently either sole sourced or single sourced.

Research and Development

Our SMRT technology requires the blending of a number of unique disciplines, namely nanofabrication, physics, photonics, optics, molecular biology, engineering, signal processing, high performance computing, and bioinformatics. Our research and development team is a blend of these disciplines creating a single, cross-functional /operating unit. We have also established productive working relationships with technology industry leaders, as well as leading academic centers, to augment and complement our internal research and development efforts. Research and development expenses incurred were $67.6 million, $60.4 million and $48.2 million during 2016, 2015 and 2014, respectively. We plan to continue our investment in research and development to enhance the performance and expand the application of our current products, and introduce additional products based on our SMRT technology. Our goals include further improvements in sequencing read length and mappable data per SMRT Cell, chemistry and software enhancements, and enhancements in sample preparation and bioinformatics tools that take advantage of the capabilities of our products. In addition, our engineering teams will continue their focus on increasing instrument component and system reliability, reducing costs, and implementing additional system flexibility and versatility through the enhancement of existing products and development of new products.

Intellectual Property

Developing and maintaining a strong intellectual property position is an important element of our business. We have sought, and will continue to seek, patent protection for our SMRT technology, for improvements to our SMRT technology, as well as for any of our other technologies where we believe such protection will be advantageous.

Our current patent portfolio, including patents exclusively licensed to us, is directed to various technologies, including SMRT nucleic acid sequencing and other methods for analyzing biological samples, ZMW arrays, surface treatments, phospholinked nucleotides and other reagents for use in nucleic acid sequencing, optical components and systems, processes for identifying nucleotides within nucleic acid

sequences and processes for analysis and comparison of nucleic acid sequence data. Some of the patents and applications that we own, as well as some of the patents and applications that we have licensed from other parties, are subject to U.S. government march-in rights, whereby the U.S. government may disregard our exclusive patent rights on its own behalf or on behalf of third parties by imposing licenses in certain circumstances, such as if we fail to achieve practical application of the U.S. government funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, U.S. government funded inventions must be reported to the government and U.S. government funding must be disclosed in any resulting patent applications.

As of December 31, 2016, we own or hold exclusive licenses to 221 issued U.S. patents, 106 pending U.S. patent applications, 133 granted foreign patents and 81 pending foreign patent applications, including foreign counterparts of U.S. patent and patent applications. The full term of the issued U.S. patents will expire between 2019 and 2034. We also have non-exclusive patent licenses with various third parties to supplement our own large and robust patent portfolio.

Of our exclusively licensed patent applications, 20 issued U.S. patents, one pending U.S. patent application, 14 granted foreign patents and one pending foreign patent application are licensed to us by the Cornell Research Foundation, which manages technology transfers on behalf of Cornell University. We have also entered into a license agreement with Indiana University Research and Technology Corporation, or IURTC, for U.S. Patent No. 6,399,335, which relates to nucleoside triphosphates that include a labeling group attached through the terminal phosphate group in the triphosphate chain. We have also entered into a license agreement with GE Healthcare Bio-Sciences Corp, or GE Healthcare, for several U.S. and foreign patents and pending patent applications related to labeled nucleoside polyphosphate compounds.

In September 2013, we entered into a Development, Commercialization and License Agreement (the “Roche Agreement”) with Roche, pursuant to which we: (i) had been developing diagnostic products for clinical use including sequencing systems and consumables based on our proprietary SMRT technology; (ii) had agreed to grant to Roche an exclusive right to commercialize, and an exclusive license to sell, the developed diagnostic products for clinical use; and (iii) had agreed to manufacture and supply certain products intended for clinical use as the exclusive supplier to Roche. We received a non-refundable up-front payment of $35.0 million in 2013, and milestone payments totaling $40.0 million in 2014 and 2015 pursuant to the Roche Agreement. No further milestone payments are expected under the Roche Agreement. On December 12, 2016, we received notice from Roche that Roche had elected to terminate the Roche Agreement for convenience. The termination will become effective on February 10, 2017, which is 60 days after the date of the notice required under the Roche Agreement.

On November 2, 2016, we filed a complaint against Oxford Nanopore Technologies Ltd., Oxford Nanopore Technologies, Inc. and Metrichor, Ltd. (together, “ONT”) with the U.S. International Trade Commission (“USITC”) for patent infringement. On December 5, 2017, the USITC provided notice that an investigation had been instituted based on the complaint. We are seeking exclusionary relief with respect to several ONT products, including ONT’s MinION and PromethION devices. The complaint is based on our U.S. Patent No. 9,404,146, entitled “Compositions and methods for nucleic acid sequencing” which covers novel methods for sequencing single nucleic acid molecules using linked double-stranded nucleic acid templates, providing improved sequencing accuracy. We have notified the Commission of our intention to add a second patent in the same patent family, U.S. Patent No. 9,542,527, which was granted on January 10, 2017, to the investigation. We are seeking, among other things, an exclusion order permanently barring entry of infringing ONT products into the United States, and a cease and desist order preventing ONT from advertising and selling infringing products in the United States.

Where patent protection is difficult to obtain or difficult to enforce for a particular technological development or the technological development derives greater value from being maintained as confidential information, we seek to protect such information as trade secrets.

Competition

Given the market opportunity, there are a significant number of competing companies offering DNA sequencing equipment or consumables. These include Illumina, Inc. and Thermo Fisher Scientific, Inc. These companies currently have greater financial, technical, research and/or other resources than we do. They also have larger and more established manufacturing capabilities and marketing, sales and support functions. We expect the competition to intensify within this market as there are also several companies in the process of developing new, potentially competing technologies, products and/or services, including Oxford Nanopore Technologies Ltd. Increased competition may result in pricing pressures, which could harm our sales, profitability or market share.

In order for us to successfully compete against these companies, we will need to demonstrate that our products deliver superior performance and value as a result of our key differentiators, including single molecule, real-time resolution, the combination of very high consensus accuracy and long read lengths with the ability to detect real-time kinetic information, fast time to result and flexibility, as well as the breadth and depth of current and future products and applications.

Employees

As of December 31, 2016, we had 438 full-time employees. Of these employees, 159 were in research and development, 98 were in operations, 125 were in marketing, sales, service and support, and 56 were in general and administration. With the exception of our field-based sales and service teams, substantially all of our employees are located at our headquarters in Menlo Park, California. None of our employees are represented by labor unions or are covered by a collective bargaining agreement with respect to their employment. We have not experienced any work stoppages, and we consider our relationship with our employees to be good.

Available Information

Our website is located at www.pacb.com. The information posted on our website is not incorporated into this Current Report on Form 8-K. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to reports filed or

furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge through the "Investors" section of our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Additionally, we use our website as a channel of distribution for important company information. Important information, including press releases, analyst presentations and financial information regarding us, as well as corporate governance information, is routinely posted and accessible on the "Investor Relations" section of the website, which is accessible by clicking on the tab labeled "About Us - Investors" on our website home page. In addition, important information is routinely posted and accessible on the blog section of our website, which is accessible by clicking on the tab labeled "Blog" on our website home page, as well as our Twitter account (@pacbio). Information on or that can be accessed through our website or our Twitter account is not part of this Current Report on Form 8-K, and the inclusion of our website address is an inactive textual reference only.

RISK FACTORS

You should consider carefully the risks and uncertainties described below, together with all of the other information in this Quarterly Report on Form 8-K, which could materially affect our business, financial condition, results of operations and prospects. The risks described below are not the only risks facing us. Risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially affect our business, financial condition, results of operations and prospects.

Risks Related to Our Business

We have limited experience as a commercial company.

Our first commercial product launched in 2011 and we have had limited sales to date. As such, we have limited historical financial data upon which to base our projected revenue, planned operating expenses or upon which to evaluate our company and our commercial prospects. Furthermore, in September 2015, we launched a new nucleic acid sequencing platform, the PacBio Sequel™ System, but have made only limited deliveries of the Sequel System to date. Based on our limited experience in developing and marketing our existing products and launching new products, we may not be able to effectively:

- drive adoption of our current and future products, including the Sequel System;
- attract and retain customers for our products;
- provide appropriate levels of customer training and support for our products;
- implement an effective marketing strategy to promote awareness of our products;
- develop, manufacture and commercialize new products or achieve an acceptable return on our manufacturing or research and development efforts and expenses;
- comply with regulatory requirements applicable to our products;
- anticipate and adapt to changes in our market;
- accommodate customer expectations and demands with respect to our products, increase product adoption by our existing customers or develop new customer relationships;
- grow our market share by marketing and selling our products to new and additional market segments;
- maintain and develop strategic relationships with vendors and manufacturers to acquire necessary materials for the production of our existing or future products;
- adapt or scale our manufacturing activities to meet potential demand at a reasonable cost;
- avoid infringement and misappropriation of third-party intellectual property;
- obtain any necessary licenses to third-party intellectual property on commercially reasonable terms;
- obtain valid and enforceable patents that give us a competitive advantage or enforce existing patents;
- protect our proprietary technology; and
- attract, retain and motivate qualified personnel.

The risks noted above, especially with respect to the marketing, sales, and commercialization of our products into the markets that Roche would have addressed under the Roche Agreement, may be heightened by the recent termination of the Roche Agreement. In addition, a high percentage of our expenses is and will continue to be fixed. Accordingly, if we do not generate revenue as and when anticipated, our losses may be greater than expected and our operating results will suffer.

We have incurred losses to date, and we expect to continue to incur significant losses as we develop our business and may never achieve profitability.

We have incurred net losses since inception and we cannot be certain if or when we will produce sufficient revenue from our operations to support our costs. While we achieved profitability for the quarter ended September 30, 2015, this result was largely due to a one-time gain on lease amendments. We have incurred net losses for all other fiscal periods, and, even if profitability is achieved in the future, we

may not be able to sustain profitability on a consistent basis. We expect to continue to incur substantial losses and negative cash flow from operations for the foreseeable future.

If our products fail to achieve and sustain sufficient market acceptance, we will not generate expected revenue and our business may not succeed.

We cannot be sure that our current or future products will gain acceptance in the marketplace at levels sufficient to support our costs. Our success depends, in part, on our ability to expand the market for genetic analysis to include new applications that are not practicable with other current technologies. To accomplish this, we must successfully commercialize, and continue development of, our proprietary Single Molecule, Real-Time (SMRT®) Sequencing technology for use in a variety of life science and other applications, including uses by academic, government and clinical laboratories, as well as pharmaceutical, diagnostic, biotechnology and agriculture companies, among others. There can be no assurance that we will be successful in securing additional customers for our products. For example, we have limited experience commercializing and selling products outside of the academic and research settings, and we cannot assure you that we can successfully acquire additional customers in additional markets. Furthermore, we cannot guarantee that our products will be satisfactory to potential customers in the markets we seek to reach. These markets are new and dynamic, and there can be no assurance that they will develop as quickly as we anticipate, that they will reach their full potential or that they will be receptive to our most recently-launched product, the Sequel System. As a result, we may be required to refocus our marketing efforts, and we may have to make changes to the specifications of our products to enhance our ability to enter particular markets more quickly. Even if we are able to implement our technology successfully, we and/or our sales and distribution partners may fail to achieve or sustain market acceptance of our current or future products across the full range of our intended life science and other applications. Given the loss of Roche as a partner, we may need to either expand our internal capabilities or collaborate with other partners, or both, in order to successfully expand sales of our products in the markets we seek to reach, including the markets that Roche would have addressed under the Roche Agreement, which we may be unable to do at the scale required to support our business. If the market for our products grows more slowly than anticipated, if we are unable to successfully scale or otherwise ensure sufficient manufacturing capacity for new products to meet demand, if we are not able to successfully market and sell our products, if competitors develop better or more cost-effective products, or if we are unable to further grow our customer base or do not realize the growth with existing customers that we are expecting, our current and future sales and revenue would be materially harmed and our business may not succeed.

If we are unable to successfully develop and timely manufacture our products, including Sequel Systems and related consumables, our business may be adversely affected.

In light of the highly complex technologies involved in our products, there can be no assurance that we will be able to manufacture and commercialize our new products on a timely basis or continue providing adequate support for our existing products. The commercial success of our products, including the Sequel System, depends on a number of factors, including performance and reliability of the system, our anticipating and effectively addressing customer preferences and demands, the success of our sales and marketing efforts, effective forecasting and management of product demand, purchase commitments and inventory levels, effective management of manufacturing and supply costs, and the quality of the Sequel System, including related consumables such as SMRT Cells and reagents. Should we face delays in or discover unexpected defects during the further development or manufacturing process of Sequel System instruments or consumables, including any delays or defects in software development or product functionality, the timing and success of the rollout and scaling of the Sequel System may be significantly impacted, which may materially and negatively impact our revenue and gross margin. The ability of our customers to successfully utilize the Sequel System will also depend on our ability to deliver high quality SMRT Cells and reagents. We have designed new SMRT Cells and other consumables for the Sequel System, and our new SMRT Cells are being sourced from a prototype chip vendor. We are in the process of transferring SMRT Cell production to a high-volume manufacturer and may experience unanticipated delays, quality defects or other issues. Our production of the new SMRT Cells has previously been and may in the future be below desired levels, and we have experienced and may experience in the future manufacturing delays, product defects and SMRT Cell variability, any of which could negatively impact our ability to sell Sequel Systems or result in other material adverse effects on our business, financial condition and results of operations.

The development of our products is complex and costly. Problems in the design or quality of our products may have a material and adverse effect on our brand, business, financial condition, and operating results, and could result is us losing our certifications from the International Organization for Standardization (“ISO”). If we were to lose ISO certification, then our customers might choose not to purchase products from us and this could adversely impact our ability to develop products approved for clinical uses. Unanticipated problems with our products could divert substantial resources, which may impair our ability to support our new and existing products, and could substantially increase our costs. If we encounter development challenges or discover errors in our products late in our development cycle, we may be forced to delay product shipments or the scaling of manufacturing or supply. In particular, if the continued rollout of the Sequel System is delayed or is not successful, we may not be able to achieve an acceptable return, if any, on our substantial research and development efforts, and our business may be materially and adversely affected. The expenses or losses associated with delayed or unsuccessful product development or lack of market acceptance of our new products could materially and adversely affect our business, financial condition and results of operations.

Our research and development efforts may not result in the benefits we anticipate, and our failure to successfully market, sell, and commercialize our current and future products could have a material adverse effect on our business, financial condition and results of operations.

We have dedicated significant resources to developing our current products, including sequencing systems and consumables based on our proprietary SMRT Sequencing technology and our Sequel System. We are also engaged in substantial and complex research and development efforts, which, if successful, may result in the introduction of new products in the future. Our research and development efforts are complex and require us to incur substantial expenses. We may not be able to develop and commercialize new products, obtain regulatory approval if necessary, or achieve an acceptable return, if any, on our research and development efforts and expenses. There can also be no assurance that we will be able to develop and manufacture future products as a result of our research and development efforts, or that we will be able to market, sell and commercialize the products that result from our research and development efforts. Furthermore, in December 2016, Roche elected to terminate the Roche Agreement. We may therefore need to expand our internal capabilities or seek new partnerships or collaborations, or both, in order to successfully market, sell and commercialize the products that we have developed in the markets we seek to reach, including the markets that Roche would have addressed under the Roche Agreement.

We must successfully manage new product introductions and transitions, we may incur significant costs during these transitions, and they may not result in the benefits we anticipate.

If our products and services fail to deliver the performance or results expected by our current and future customers, or are not delivered on a timely basis, our reputation and credibility may suffer, our current and future sales and revenue may be materially harmed and our business may not succeed. For instance, if we are not able to realize the benefits we anticipate from the development and commercialization of the Sequel System or our future products, including those that may be developed for clinical uses, it could have a material adverse effect on our business, financial condition and results of operations. In addition, the introduction of future products may lead to our limiting or ceasing development of further enhancements to our existing products and consumables as we focus our resources on new products, and could result in reduced marketplace acceptance and loss of sales of our existing products, materially adversely affecting our revenue and operating results. The introduction of new products, such as the Sequel System, may also have a negative impact on our revenue in the near-term as our current and future customers may delay or cancel orders of existing products in anticipation of new products and we may also be pressured to decrease prices for our existing products. Further, we have in the past experienced, and could in the future experience difficulty in managing or forecasting customer reactions, purchasing decisions or transition requirements with respect to newly-launched products, such as the Sequel System. We could incur significant costs in completing the transition, including costs of inventory write-downs of our products, as current or future customers transition to the new Sequel System. If we do not successfully manage this product transition, our business, reputation and financial condition may be materially and adversely affected.

We rely on other companies for the manufacture of certain components and sub-assemblies and intend to outsource additional sub-assemblies in the future. We may not be able to successfully scale the manufacturing process necessary to build and test multiple products on a full commercial basis, which could materially harm our business.

Our products are complex and involve a large number of unique components, many of which require precision in manufacturing. The nature of our products requires customized components that are currently available only from a limited number of sources, and in some cases, single sources. We have chosen to source certain critical components from a single source, including suppliers for our SMRT Cells, reagents and instruments. Furthermore, we are in the process of transferring production of the SMRT Cells for our Sequel System to a high-volume manufacturer and may experience unanticipated delays or other issues in connection with such transition. If we are required to purchase these components from alternative sources, it could take several months or longer to qualify the alternative sources. If we are unable to secure a sufficient supply of these product components on a timely basis, or if these components do not meet our expectations or specifications for quality and functionality, our operations and manufacturing will be materially and adversely affected, we could be unable to meet customer demand and our business and results of operations may be materially and adversely affected.

The operations of our third-party manufacturing partners and suppliers could be disrupted by conditions unrelated to our business or operations or that are beyond our control, including but not limited to international trade restrictions or changes resulting from factors beyond our control. If our manufacturing partners or suppliers are unable or fail to fulfill their obligations to us for any reason, we may not be able to manufacture our products and satisfy customer demand or our obligations under sales agreements in a timely manner, and our business could be harmed as a result. Our current manufacturing process is characterized by long lead times between the placement of orders for and delivery of our products. If we have received insufficient components to manufacture our products on a timely basis to meet customer demand, our sales and our gross margin may be adversely affected and our business could be materially harmed. If we are unable to reduce our manufacturing costs and establish and maintain reliable, high-volume manufacturing suppliers as we scale our operations, our business could be materially harmed.

We may be unable to consistently manufacture our instruments and consumable kits, including SMRT Cells, to the necessary specifications or in quantities necessary to meet demand at an acceptable cost.

In order to successfully generate revenue from our products, we need to supply our customers with products that meet their expectations for quality and functionality in accordance with established specifications. Our customers have previously experienced variability

in the performance of our instruments and SMRT Cells. Moreover, we are manufacturing a new version of our SMRT Cells for the Sequel System, and are in the process of simultaneously moving our in-house manufacturing facilities and scaling up manufacturing capacity for our products. In connection with this process, we may experience delays, qualities issues or other difficulties leading to customer dissatisfaction with our products. Our production of new SMRT Cells has initially been and may in the future be below desired levels and we have experienced and may experience in the future manufacturing delays, product defects and SMRT Cell variability, especially as we transfer production of our SMRT Cells to a high-volume manufacturer. There is no assurance that we will be able to manufacture our products so that they consistently achieve the product specifications and quality that our customers expect, including any products developed for clinical uses. Problems in the design or quality of our products may have a material adverse effect on our brand, business, financial condition, and operating results, and could result is us losing our ISO certifications. If we were to lose our ISO certification, then our customers might choose not to purchase products from us. There is also no assurance that we will be able to increase manufacturing yields and decrease costs, or that we will be successful in forecasting customer demand or manufacturing and supply costs. Furthermore, we may not be able to increase manufacturing to meet anticipated demand or may experience downtime in our existing manufacturing facilities. An inability to manufacture products and components that consistently meet specifications, in necessary quantities and at commercially acceptable costs, will have a negative impact, and may have a material adverse effect, on our business, financial condition and results of operations.

Rapidly changing technology in life sciences and diagnostics could make our products obsolete unless we continue to develop and commercialize new and improved products and pursue new market opportunities.

Our industry is characterized by rapid and significant technological changes, frequent new product introductions and enhancements and evolving industry standards. Our future success will depend on our ability to continually improve our products, to develop and introduce new products that address the evolving needs of our customers on a timely and cost-effective basis and to pursue new market opportunities. These new market opportunities may be outside the scope of our proven expertise or in areas where the market demand is unproven, and new products and services developed by us may not gain market acceptance. Our inability to develop and introduce new products and to gain market acceptance of the Sequel System and other new products could harm our future operating results. Unanticipated difficulties or delays in replacing existing products with new products or in commercializing the Sequel System or other new or improved products in sufficient quantities to meet customer demand could diminish future demand for our products and harm our future operating results.

Increased market adoption of our products by customers may depend on the availability of sample preparation and informatics tools, some of which may be developed by third parties.

Our commercial success may depend in part upon the development of sample preparation and software and informatics tools by third parties for use with our products. We cannot guarantee that third parties will develop tools that our current and future customers will find useful with our products. A lack of complementary sample preparation and informatics tools may impede the adoption of our products and may materially and adversely impact our business.

We operate in a highly competitive industry and if we are not able to compete effectively, our business and operating results will likely be harmed.

Some of our current competitors, including Illumina, Inc. and Thermo Fisher Scientific Inc., as well as other potential competitors, have greater name recognition, more substantial intellectual property portfolios, longer operating histories, significantly greater financial, technical, research and/or other resources, more experience in new product development, larger and more established manufacturing capabilities and marketing, sales and support functions, and/or more established distribution channels to deliver products to customers than we do. These competitors may be able to respond more quickly and effectively than we can to new or changing opportunities, technologies, standards or customer requirements. In light of these advantages, even if our technology is more effective than the products or service offerings of our competitors, current and potential customers might purchase competitive products and services instead of our products.

There are also several companies that are in the process of developing or have already developed new, potentially competing technologies, products and/or services, including Oxford Nanopore Technologies Ltd., against whom we have filed a complaint with the U.S. International Trade Commission for patent infringement. Roche has also developed and commercialized its 454 Life Sciences sequencing systems and is developing alternative and potentially competing sequencing products through its acquisition of Genia Technologies. Increased competition may result in pricing pressures, which could harm our sales, profitability or market share. Our failure to further enhance our existing products and to introduce new products to compete effectively could materially and adversely affect our business, financial condition or results of operations.

We may be unable to successfully increase sales of our products.

Our ability to achieve profitability depends on our ability to attract customers for our current and future products, and we may be unable to effectively market or sell our products, or find appropriate partners to do so. To perform sales, marketing, distribution and customer support functions successfully, we face a number of risks, including:

- our ability to attract, retain and manage the sales, marketing and service personnel necessary to expand market acceptance for our technologies;
- availability of potential sales partners to sell our technologies, and our ability to attract and retain such sales partners;
- the time and cost of maintaining and growing a specialized sales, marketing and service force for a particular application, which may be difficult to justify in light of the revenue generated; and

· our sales, marketing and service force may be unable to execute successful commercial activities.

We have enlisted and may continue to enlist third parties to assist with sales, distribution and customer support. There is no guarantee that we will be successful in attracting desirable sales and distribution partners, that we will be able to enter into arrangements with such partners on terms favorable to us or that we will be able to retain such partners on a going forward basis. If our sales and marketing efforts, or those of any of our third-party sales and distribution partners, are not successful, our technologies and products may not gain market acceptance, which could materially impact our business operations.

We plan to raise additional financing to fund our existing operations. Equity and debt securities we issue may have rights senior to common stockholders and additional equity financing will dilute the holdings of current stockholders.

We plan to raise additional funds through public or private debt or equity financing. Additional funds may not be available on terms acceptable to us or at all, particularly in light of restrictions under our debt agreement. We have incurred and may further incur additional debt. Debt holders have rights senior to common stockholders to make claims on our assets and the terms of our existing debt agreement restrict certain activities, including our ability to pay dividends on our common stock. To the extent that we raise additional funds through the sale of our common stock, downward fluctuations in our stock price could adversely affect such fundraising efforts. Furthermore, fundraising through sales of additional shares of common stock or other equity securities will have a dilutive effect on our existing investors.

Our indebtedness could adversely affect our financial condition and prevent us from fulfilling our obligations.

Our net losses since inception and our expectation of incurring substantial losses and negative cash flow for the foreseeable future, combined with our existing indebtedness, could:

· make it more difficult for us to satisfy our obligations, including under our existing debt agreement;

· increase our vulnerability to general adverse economic and industry conditions;

· limit our ability to fund future working capital, capital expenditures, research and development and other business opportunities;

· require us to dedicate a substantial portion of our cash flow from operations to service payments on our indebtedness;

· increase the volatility of the price of our common stock;

· limit our flexibility to react to changes in our business and the industry in which we operate;

· place us at a competitive disadvantage to our competitors that have less or no indebtedness; and

· limit, along with the financial and other restrictive covenants in our indebtedness, among other things, our ability to borrow additional funds.

Our existing debt contains covenants which may adversely impact our business and our failure to comply with such covenants could cause our outstanding indebtedness to become immediately payable.

Our existing debt contains various affirmative and negative covenants, including restrictions on our and our subsidiaries' ability to incur additional indebtedness or liens on our assets. These covenants impose significant operating and financial restrictions on us, including restrictions on our ability to take certain actions that may be in our best interests.

A breach of any of the covenants contained in our debt could result in an event of default. If an event of default exists, debt holders could elect to declare all amounts outstanding under the debt to be immediately due and payable. If we are unable to repay our indebtedness when due and payable, debt holders could proceed against the collateral granted to them to secure such indebtedness. We have pledged substantially all of our property and interests in property, including our intellectual property, as collateral under our existing debt. If the debt holders accelerate the repayment of our indebtedness, we may not have sufficient funds to make such repayment, which could have a material adverse effect on our liquidity and ability to conduct our business.

In addition, at the election of the holders representing a majority of the aggregate principal amount of the outstanding notes issued pursuant to our existing debt agreement, the holders may elect to receive 25% of the net proceeds from any financing that includes an equity component, including, without limitation, the sale or issuance of our common stock, options, warrants or other securities convertible or exchangeable for shares of our common stock, as partial payment of the notes. This right is subject to certain exceptions set forth in our existing debt agreement. To the extent we raise additional capital in the future through the sale of common stock under any future "at-the-market" offering or through other financing activities, we may be obligated, at the election of the holders of the notes, to pay 25% of the net proceeds from any such financing activities as partial payment of the notes.

Our products are highly complex, have recurring support requirements and could have unknown defects or errors, which may give rise to claims against us or divert application of our resources from other purposes.

Products using our SMRT Sequencing technology are highly complex and may develop or contain undetected defects or errors. Our customers have in the past experienced reliability issues with our products, and we have only recently launched the Sequel System, such that support costs are difficult to predict. Despite testing, defects or errors may arise in our products, which could result in a failure to maintain or increase market acceptance of our products, diversion of development resources, injury to our reputation and increased warranty, service and

maintenance costs. New products or enhancements to our existing products in particular may contain undetected errors or performance problems that are discovered only after delivery to customers. If our products have reliability or other quality issues or require unexpected levels of support in the future, the market acceptance and utilization of our products may not grow to levels sufficient to support our costs and our reputation and business could be harmed. We generally ship our sequencing instruments with one year of service included in the purchase price with an option to purchase one or more additional years of service. We also provide a warranty for our consumables, which is generally limited to replacing, or at our option, giving credit for any consumable with defects in material or workmanship. Defects or errors in our products may also discourage customers from purchasing our products. The costs incurred in correcting any defects or errors may be substantial and could materially and adversely affect our operating margins. If our service and support costs increase, our business and operations may be materially and adversely affected.

In addition, such defects or errors could lead to the filing of product liability claims against us or against third parties who we may have an obligation to indemnify against such claims, which could be costly and time-consuming to defend and result in substantial damages. Although we have product liability insurance, any product liability insurance that we have or procure in the future may not protect our business from the financial impact of a product liability claim. Moreover, we may not be able to obtain adequate insurance coverage on acceptable terms. Any insurance that we have or obtain will be subject to deductibles and coverage limits. A product liability claim could have a serious adverse effect on our business, financial condition and results of operations.

We depend on the continuing efforts of our senior management team and other key personnel. If we lose members of our senior management team or other key personnel or are unable to successfully retain, recruit and train qualified scientists, engineers and other personnel, our ability to maintain and develop our products could be harmed and we may be unable to achieve our goals.

Our future success depends upon the continuing services of members of our senior management team and scientific and engineering personnel. In particular, our scientists and engineers are critical to our future technological and product innovations and we will need to hire additional qualified personnel. Our industry, particularly in the San Francisco Bay Area, is characterized by high demand and intense competition for talent, and the turnover rate can be high. We compete for qualified management and scientific personnel with other life science companies, academic institutions and research institutions, particularly those focusing on genomics. Our employees could leave our company with little or no prior notice and would be free to work for a competitor. If one or more of our senior executives or other key personnel were unable or unwilling to continue in their present positions, we may not be able to replace them easily or at all, and other senior management may be required to divert attention from other aspects of the business. In addition, we do not have “key person” life insurance policies covering any member of our management team or other key personnel. The loss of any of these individuals or any inability to attract or retain qualified personnel, including scientists, engineers and others, could prevent us from pursuing collaborations and materially and adversely affect our support of existing products, product development and introductions, business growth prospects, results of operations and financial condition.

A significant portion of our potential sales depends on customers’ spending budgets that may be subject to significant and unexpected variation which could have a negative effect on the demand for our products.

Our instruments represent significant capital expenditures for our customers. Potential customers for our current or future products include academic and government institutions, genome centers, medical research institutions, clinical laboratories, pharmaceutical, agricultural, biotechnology, diagnostic and chemical companies. Their spending budgets can have a significant effect on the demand for our products. Spending budgets are based on a wide variety of factors, including the allocation of available resources to make purchases, funding from government sources which is highly uncertain and subject to change, the spending priorities among various types of research equipment and policies regarding capital expenditures during economically uncertain periods. Any decrease in capital spending or change in spending priorities of our current and potential customers could significantly reduce the demand for our products. Any delay or reduction in purchases by potential customers or our inability to forecast fluctuations in demand could harm our future operating results.

We may not be able to convert our orders in backlog into revenue.

Our backlog represents product orders from our customers that we have confirmed and for which we have not yet recognized revenue. We may not receive revenue from these orders, and the order backlog we report may not be indicative of our future revenue.

Many events can cause an order to be delayed or not completed at all, some of which may be out of our control. If we delay fulfilling customer orders or if customers reconsider their orders, those customers may seek to cancel or modify their orders with us. Customers may otherwise seek to cancel or delay their orders even if we are prepared to fulfill them. If our orders in backlog do not result in sales, our operating results may suffer.

Delivery of our products could be delayed or disrupted by factors beyond our control, and we could lose customers as a result.

We rely on third-party carriers for the timely delivery of our products. As a result, we are subject to carrier disruptions and increased costs that are beyond our control. Any failure to deliver products to our customers in a safe and timely manner may damage our reputation and brand and could cause us to lose customers. If our relationship with any of these third-party carriers is terminated or impaired or if any of these carriers are unable to deliver our products, the delivery and acceptance of our products by our customers may be delayed, which could harm

our business and financial results. The failure to deliver our products in a safe and timely manner may harm our relationship with our customers, increase our costs and otherwise disrupt our operations.

We are, and may become, subject to governmental regulations that may impose burdens on our operations, and the markets for our products may be narrowed.

We are subject, both directly and indirectly, to the adverse impact of government regulation of our operations and markets. For example, export of our instruments may be subject to strict regulatory control in a number of jurisdictions. We have expanded and are continuing to expand the international jurisdictions into which we supply products, which increase the risks surrounding governmental regulations relating to our business. The failure to satisfy export control criteria or to obtain necessary clearances could delay or prevent shipment of products, which could materially and adversely affect our revenue and profitability. Moreover, the life sciences industry, which is expected to be one of the primary markets for our technology, has historically been heavily regulated. There are, for example, laws in several jurisdictions restricting research in genetic engineering, which may narrow our markets. Given the evolving nature of this industry, legislative bodies or regulatory authorities may adopt additional regulations that may adversely affect our market opportunities. Additionally, if ethical and other concerns surrounding the use of genetic information, diagnostics or therapies become widespread, there may be less demand for our products.

Our business is also directly affected by a wide variety of government regulations applicable to business enterprises generally and to companies operating in the life science industry in particular. Failure to comply with government regulations or obtain or maintain necessary permits and licenses could result in a variety of fines or other censures or an interruption in our business operations which may have a negative impact on our ability to generate revenue and the cost of operating our business. In addition, changes to laws and government regulations could cause a material adverse effect on our business as we will need to adapt our business to comply with such changes. For example, a governmental prohibition on the use of human *in vitro* diagnostics would adversely impact our commercialization of products on which we have expended significant research and development resources, which would in turn have a material adverse impact on our business and prospects.

Our products could become subject to regulation by the U.S. Food and Drug Administration or other domestic and international regulatory agencies, which could increase our costs and impede or delay our commercialization efforts, thereby materially and adversely affecting our business and results of operations.

Our products are not currently subject to U.S. Food and Drug Administration (“FDA”) clearance or approval since they are not intended for use in the diagnosis or treatment of disease. However, in the future, certain of our products or related applications, such as those that may be developed for clinical uses, could be subject to FDA regulation, or the FDA’s regulatory jurisdiction could be expanded to include our products. Even where a product is exempted from FDA clearance or approval, the FDA may impose restrictions as to the types of customers to which we or our partners can market and sell our products. Such regulation and restrictions may materially and adversely affect our business, financial condition and results of operations. In the event that we fail to obtain and maintain necessary regulatory clearances or approvals for products that we develop for clinical uses, or if clearances or approvals for future products and indications are delayed or not issued, our commercial operations may be materially harmed. Furthermore, even if we are granted regulatory clearances or approvals, they may include significant limitations on the indicated uses for the product, which may limit the market for the product. We do not have experience in obtaining FDA approvals and no assurance can be given that we will be able to obtain or to maintain such approvals. Furthermore, any approvals that we may obtain can be revoked if safety or efficacy problems develop.

Many countries have laws and regulations that could affect our products, such as 510(k) clearances, premarket approvals or CE Mark requirements, and failure to adhere to applicable statutory or regulatory requirements by us or our business partners would have a material adverse effect on our operations and financial condition. The number and scope of these requirements are increasing. Unlike many of our competitors, this is an area where we do not have expertise. We, or our other third-party sales and distribution partners, may not be able to obtain regulatory approvals in such countries or may incur significant costs in obtaining or maintaining our foreign regulatory approvals. In addition, the export by us of certain of our products, which have not yet been cleared for domestic commercial distribution, may be subject to FDA or other export restrictions. Any action brought against us for violations of these laws or regulations, even if successfully defended, could cause us to incur significant legal expenses and divert our management’s attention from the operation of our business.

Doing business internationally creates operational and financial risks for our business.

We currently conduct operations in various countries and jurisdictions, and continue to expand to new international jurisdictions. For example, in 2016, we started selling into several new countries directly and through distribution partners, including Mexico and Israel, where we or our distribution partners may be subject to additional regulations and increased diversion of management time and efforts. Conducting and launching operations on an international scale requires close coordination of activities across multiple jurisdictions and time zones and consumes significant management resources. If we fail to coordinate and manage these activities effectively, our business, financial condition or results of operations could be materially and adversely affected and failure to comply with laws and regulations applicable to business operations in foreign jurisdictions may also subject us to significant liabilities and other penalties. International operations entail a variety of other risks, including, without limitation:

- challenges in staffing and managing foreign operations;

- tariffs and other trade barriers;

- changes in social, political and economic conditions or in laws, regulations and policies governing foreign trade, manufacturing, development and investment both domestically as well as in the other countries and jurisdictions into which we sell our products, including as a result of the referendum held in the United Kingdom approving the separation of the United Kingdom as a member of the European Union;

- difficulties in obtaining export licenses or in overcoming other trade barriers and restrictions resulting in delivery delays;

- potential increases on tariffs or restrictions on trade generally; and

- significant taxes or other burdens of complying with a variety of foreign laws.

In conducting our international operations, we are subject to U.S. laws relating to our international activities, such as the Foreign Corrupt Practices Act of 1977, as well as foreign laws relating to our activities in other countries, such as the United Kingdom Bribery Act of 2010. Failure to comply with these laws may subject us to claims or financial and/or other penalties in the United States and/or foreign countries that could materially and adversely impact our operations or financial condition. These risks have become increasingly prevalent as we have expanded our sales into countries that are generally recognized as having a higher risk of corruption.

We face risks related to the current global economic environment, which could delay or prevent our customers from purchasing our products, which could in turn harm our business, financial condition and results of operations. The state of the global economy continues to be uncertain. The current global economic conditions and uncertain credit markets and concerns regarding the availability of credit pose a risk that could impact customer demand for our products, as well as our ability to manage normal commercial relationships with our customers, suppliers and creditors, including financial institutions. If the current global economic environment deteriorates, our business could be negatively affected.

Moreover, changes in the value of the relevant currencies may affect the cost of certain items required in our operations. Changes in currency exchange rates may also affect the relative prices at which we are able sell products in the same market. Our revenue from international customers may be negatively impacted as increases in the U.S. dollar relative to our international customers' local currencies could make our products more expensive, impacting our ability to compete or as a result of financial or other instability in such locations which could result in decreased sales of our products. Our costs of materials from international suppliers may also increase as the value of the U.S. dollar decreases relative to their local currency. Foreign policies and actions regarding currency valuation could result in actions by the United States and other countries to offset the effects of such fluctuations. Such actions may materially and adversely impact our financial condition and results of operations.

Violations of complex foreign and U.S. laws and regulations could result in fines and penalties, criminal sanctions against us, our officers, or our employees, prohibitions on the conduct of our business and on our ability to offer our products and services in one or more countries, and could also materially affect our brand, our international growth efforts, our ability to attract and retain employees, our business, and our operating results. Even if we implement policies or procedures designed to ensure compliance with these laws and regulations, there can be no assurance that our distribution partners, our employees, contractors, or agents will not violate our policies and subject us to potential claims or penalties.

If we fail to comply with healthcare and other governmental regulations, we could face substantial penalties and our business, results of operations and financial condition could be adversely affected.

The products that we may develop for clinical uses may be highly regulated, and there can be no assurance that the regulatory environment in which we would operate will not change significantly and adversely in the future. Any arrangements with physicians, hospitals and clinics may expose us to broadly applicable fraud and abuse and other laws and regulations that may restrict the financial arrangements and relationships through which we market, sell and distribute our products and services. Our employees, consultants, and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements. Federal and state healthcare laws and regulations that may affect our ability to conduct business, include, without limitation:

- federal and state laws and regulations regarding billing and claims payment applicable to products that we may develop for clinical uses, and regulatory agencies enforcing those laws and regulations;

- the federal Anti-Kickback Statute, which prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs;

- the federal False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, false claims, or knowingly using false statements, to obtain payment from the federal government;

- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- the FCPA, the U.K. Bribery Act of 2010, and other local anti-corruption laws that apply to our international activities;

- the federal Physician Payment Sunshine Act, or Open Payments, created under the Affordable Care Act, and its implementing regulations, which requires manufacturers of drugs, medical devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the U.S. Department of

Health and Human Services, or HHS, information related to payments or other transfers of value made to licensed physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, which impose certain requirements relating to the privacy, security and transmission of individually identifiable health information; HIPAA also created criminal liability for knowingly and willfully falsifying or concealing a material fact or making a materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal physician self-referral prohibition, commonly known as the Stark Law; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third party payor, including commercial insurers, and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or Affordable Care Act, was enacted in 2010. The Affordable Care Act, among other things, amends the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our activities could be subject to challenge under one or more of such laws. Any action brought against us for violations of these laws or regulations, even successfully defended, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. We may be subject to private "qui tam" actions brought by individual whistleblowers on behalf of the federal or state governments, with potential liability under the federal False Claims Act including mandatory treble damages and significant per-claim penalties.

The growth of our business and sales organization and our expansion outside of the United States may increase the potential of violating these laws. The risk of our being found in violation of these or other laws and regulations is further increased by the fact that many have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action brought against us for violation of these or other laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. If our operations are found to be in violation of any of the federal, state and foreign laws described above or any other current or future fraud and abuse or other healthcare laws and regulations that apply to us, we may be subject to penalties, including significant criminal, civil, and administrative penalties, damages, fines, imprisonment, for individuals, exclusion from participation in government programs, such as Medicare and Medicaid, and we could be required to curtail or cease certain of our operations. Any of the foregoing consequences could seriously harm our business and our financial results.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired, which would adversely affect our business and our stock price.

Ensuring that we have adequate internal financial and accounting controls and procedures in place to produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be evaluated frequently. We may in the future discover areas of our internal financial and accounting controls and procedures that need improvement. Operating as a public company requires sufficient resources within the accounting and finance functions in order to produce timely financial information, ensure the level of segregation of duties, and maintain adequate internal control over financial reporting customary for a U.S. public company.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with U.S. GAAP. Our management does not expect that our internal control over financial reporting will prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud, if any, within our company will have been detected.

Pursuant to Section 404 of the Sarbanes-Oxley Act, we perform periodic evaluations of our internal control over financial reporting. While we have in the past performed this evaluation and concluded that our internal control over financial reporting was operating effectively, there can be no assurance that in the future material weaknesses or significant deficiencies will not exist or otherwise be discovered. In addition, if we are unable to produce accurate financial statements on a timely basis, investors could lose confidence in the reliability of our financial statements, which could cause the market price of our common stock to decline and make it more difficult for us to finance our operations and growth.

Our ability to use net operating losses to offset future taxable income may be subject to substantial limitations.

Under Section 382 of the Internal Revenue Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses ("NOLs") to offset future taxable income. We believe that we have had one or more

ownership changes, as a result of which our existing NOLs are currently subject to limitation. Future changes in our stock ownership could result in additional ownership changes under Section 382. We may not be able to utilize a material portion of our NOLs even if we attain profitability.

Our sales cycle is unpredictable and lengthy, which makes it difficult to forecast revenue and may increase the magnitude of quarterly or annual fluctuations in our operating results.

The sales cycle for our sequencing instruments is lengthy because they represent a major capital expenditure and generally require the approval of our customers' senior management. This may contribute to substantial fluctuations in our quarterly or annual operating results, particularly during the periods in which our sales volume is low. Factors that may cause fluctuations in our quarterly or operating results include, without limitation, market acceptance for our products; our ability to attract new customers; publications of studies by us, competitors or third parties; the timing and success of new product introductions by us or our competitors or other changes in the competitive dynamics of our industry, such as consolidation; the amount and timing of our costs and expenses; changes in our pricing policies or those of our competitors; general economic, industry and market conditions; the regulatory environment; expenses associated with warranty costs or unforeseen product quality issues; the hiring, training and retention of key employees, including our ability to grow our sales organization; litigation or other claims against us for intellectual property infringement or otherwise; our ability to obtain additional financing as necessary; and changes or trends in new technologies and industry standards. Because of these fluctuations, it is likely that in some future quarters our operating results will fall below the expectations of securities analysts or investors. If that happens, the market price of our stock would likely decrease. Past fluctuations in our quarterly and annual operating results have resulted in decreases in our stock price. Such fluctuations also mean that investors may not be able to rely on our operating results in any particular period as an indication of future performance. Sales to existing customers and the establishment of a business relationship with other potential customers is a lengthy process, generally taking several months and sometimes longer. Following the establishment of the relationship, the negotiation of purchase terms can be time-consuming, and a potential customer may require an extended evaluation and testing period. Due to the limited sales of the Sequel System that we have had to date, we cannot be sure what the sales cycle will be for the Sequel System. In anticipation of product orders, we may incur substantial costs before the sales cycle is complete and before we receive any customer payments. As a result, in the event that a sale is not completed or is canceled or delayed, we may have incurred substantial expenses, making it more difficult for us to become profitable or otherwise negatively impacting our financial results. Furthermore, because of our lengthy sales cycle, the realization of revenue from our selling efforts may be substantially delayed, our ability to forecast our future revenue may be more limited and our revenue may fluctuate significantly from quarter to quarter.

Our operations involve the use of hazardous materials, and we must comply with environmental, health and safety laws, which can be expensive and may adversely affect our business, operating results and financial condition.

Our research and development and manufacturing activities involve the use of hazardous materials, including chemicals and biological materials, and some of our products include hazardous materials. Accordingly, we are subject to federal, state, local and foreign laws, regulations and permits relating to environmental, health and safety matters, including, among others, those governing the use, storage, handling, exposure to and disposal of hazardous materials and wastes, the health and safety of our employees, and the shipment, labeling, collection, recycling, treatment and disposal of products containing hazardous materials. Liability under environmental laws and regulations can be joint and several and without regard to fault or negligence. For example, under certain circumstances and under certain environmental laws, we could be held liable for costs relating to contamination at our or our predecessors' past or present facilities and at third-party waste disposal sites. We could also be held liable for damages arising out of human exposure to hazardous materials. There can be no assurance that violations of environmental, health and safety laws will not occur as a result of human error, accident, equipment failure or other causes. The failure to comply with past, present or future laws could result in the imposition of substantial fines and penalties, remediation costs, property damage and personal injury claims, investigations, the suspension of production or product sales, loss of permits or a cessation of operations. Any of these events could harm our business, operating results and financial condition. We also expect that our operations will be affected by new environmental, health and safety laws and regulations on an ongoing basis, or more stringent enforcement of existing laws and regulations. New laws or changes to existing laws may result in additional costs and may increase penalties associated with violations or require us to change the content of our products or how we manufacture them, which could have a material adverse effect on our business, operating results and financial condition.

Our facilities in California are located near earthquake faults, and the occurrence of an earthquake or other catastrophic disaster could cause damage to our facilities and equipment, which could require us to cease or curtail operations.

Our facilities in the San Francisco Bay Area are located near earthquake fault zones and are vulnerable to damage from earthquakes. We are also vulnerable to damage from other types of disasters, including fire, floods, power loss, communications failures and similar events. If any disaster were to occur, our ability to operate our business at our facilities would be seriously, or potentially completely, impaired. In addition, the nature of our activities could cause significant delays in our research programs and commercial activities and make it difficult for us to recover from a disaster. The insurance we maintain may not be adequate to cover our losses resulting from disasters or other business interruptions. Accordingly, an earthquake or other disaster could materially and adversely harm our ability to conduct business.

Our ability to successfully manage our transition to our new headquarters could result in a material adverse effect on our business or operations if we underestimate the costs of the transition, experience delays or quality issues with our manufacturing, or if internal measures to mitigate these risks are not effective.

We are in the process of transitioning to our new headquarters in Menlo Park, California. The transition may involve unanticipated delays, which could materially impact our desired commercial timelines and there is no assurance that we will be able to move into our new headquarters without any material interruption to our business. The successful transition of our headquarters, including the transition of our manufacturing facilities, is largely dependent upon the cooperation and continued performance of both our current and future landlords, as well as third-party contractors who are preparing certain shell improvements and tenant improvements. During the transition period, we must successfully establish and implement procedures to ensure that our current and future manufacturing facilities meet our quality standards while maintaining a reasonable cost structure. In addition, after our new manufacturing facilities have been qualified, it may take a considerable period of time to commence volume production. We have already devoted significant expenses and resources in connection with the transition, and there is no assurance that we can manage the transition successfully.

In addition, the transition to our new headquarters may delay or disrupt our ability to perform critical functions, distract our management and employees or result in unanticipated expenses, all of which could negatively affect our business, at least in the near term. There may also be additional costs associated with running separate manufacturing facilities until our in-house manufacturing has been relocated to the new headquarters, and such costs may exceed our projections. If the transition does not go as expected, in addition to other issues noted above, we could experience delayed shipments of products, unexpected cost overruns or quality issues, or loss of our ISO certifications, each of which could have a material adverse effect on our business, operating results and business reputation. Moreover, in the event that we breach any of our current Menlo Park facility real property leases and fail to cure such breach within the time permitted, the landlord would have no obligation to make the final payment due to us under the leases, as amended, as consideration for our agreement to amend the leases.

Ethical, legal, privacy and social concerns or governmental restrictions surrounding the use of genetic information could reduce demand for our technology.

Our products may be used to provide genetic information about humans, agricultural crops and other living organisms. The information obtained from our products could be used in a variety of applications which may have underlying ethical, legal, privacy and social concerns, including the genetic engineering or modification of agricultural products or testing for genetic predisposition for certain medical conditions. Governmental authorities could, for safety, social or other purposes, call for limits on or regulation of the use of genetic testing. Such concerns or governmental restrictions could limit the use of our products, which could have a material adverse effect on our business, financial condition and results of operations.

Disruption of critical information technology systems or material breaches in the security of our systems could harm our business, customer relations and financial condition.

Information technology (“IT”) helps us to operate efficiently, interface with customers, maintain financial accuracy and efficiently and accurately produce our financial statements. IT systems are used extensively in virtually all aspects of our business, including sales forecast, order fulfillment and billing, customer service, logistics, and management of data from running samples on our products. Our success depends, in part, on the continued and uninterrupted performance of our IT systems. IT systems may be vulnerable to damage from a variety of sources, including telecommunications or network failures, power loss, natural disasters, human acts, computer viruses, computer denial-of-service attacks, unauthorized access to customer or employee data or company trade secrets, and other attempts to harm our systems. Certain of our systems are not redundant, and our disaster recovery planning is not sufficient for every eventuality. Despite any precautions we may take, such problems could result in, among other consequences, disruption of our operations, which could harm our reputation and financial results.

If we do not allocate and effectively manage the resources necessary to build and sustain the proper IT infrastructure, we could be subject to transaction errors, processing inefficiencies, loss of customers, business disruptions or loss of or damage to intellectual property through security breach. If our data management systems do not effectively collect, store, process and report relevant data for the operation of our business, whether due to equipment malfunction or constraints, software deficiencies or human error, our ability to effectively plan, forecast and execute our business plan and comply with applicable laws and regulations will be impaired, perhaps materially. Any such impairment could materially and adversely affect our reputation, financial condition, results of operations, cash flows and the timeliness with which we report our internal and external operating results.

Security breaches and other disruptions could compromise our information and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our customers, suppliers and business partners, and personally identifiable information of our customers and employees, in our data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our IT infrastructure may be vulnerable to attacks by hackers, computer viruses, malicious codes, unauthorized access attempts, and cyber- or phishing-attacks, or breached due to employee error, malfeasance, faulty password management or

other disruptions. Third parties may attempt to fraudulently induce employees or other persons into disclosing user names, passwords or other sensitive information, which may in turn be used to access our IT systems, commit identity theft or carry out other unauthorized or illegal activities. Any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disruption of our operations and damage to our reputation, which could divert our management's attention from the operation of our business and materially and adversely affect our business, revenues and competitive position. Moreover, we may need to increase our efforts to train our personnel to detect and defend against cyber- or phishing-attacks, which are becoming more sophisticated and frequent, and we may need to implement additional protective measures to reduce the risk of potential security breaches, which could cause us to incur significant additional expenses.

Regulations related to conflict minerals has caused us to incur, and will continue to cause us to incur, additional expenses and could limit the supply and increase the costs of certain materials used in the manufacture of our products.

We are subject to requirements under the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 that require us to conduct diligence, and report whether or not our products contain conflict minerals. The implementation of these requirements could adversely affect the sourcing, availability and pricing of the materials used in the manufacture of components used in our products. Furthermore, the complex nature of our products requires components and materials that may be available only from a limited number of sources and, in some cases, from only a single source. We have incurred, and will continue to incur, additional costs to comply with the disclosure requirements, including costs related to conducting diligence procedures to determine the sources of conflict minerals that may be used or necessary to the production of our products and, if applicable, potential changes to components, processes or sources of supply as a consequence of such verification activities. We may face reputational harm if we determine that certain of our products contain minerals that are not determined to be conflict free or if we are unable to alter our processes or sources of supply to avoid using such materials. Reputational harm could materially and adversely affect our business, financial condition or results of operations.

Risks Related to Our Intellectual Property

Failure to secure patent or other intellectual property protection for our products and improvements to our products may reduce our ability to maintain any technological or competitive advantage over our current and potential competitors.

Our ability to protect and enforce our intellectual property rights is uncertain and depends on complex legal and factual questions. Our ability to establish or maintain a technological or competitive advantage over our competitors may be diminished because of these uncertainties. For example:

- we or our licensors might not have been the first to make the inventions covered by each of our pending patent applications or issued patents;
- we or our licensors might not have been the first to file patent applications for these inventions;
- it is possible that neither our pending patent applications nor the pending patent applications of our licensors will result in issued patents;
- the scope of the patent protection we or our licensors obtain may not be sufficiently broad to prevent others from practicing our technologies, developing competing products, designing around our patented technologies or independently developing similar or alternative technologies;
- our and our licensors' patent applications or patents have been, are and may in the future be, subject to interference, opposition or similar administrative proceedings, which could result in those patent applications failing to issue as patents, those patents being held invalid or the scope of those patents being substantially reduced;
- we or our partners may not adequately protect our trade secrets;
- we may not develop additional proprietary technologies that are patentable; or
- the patents of others may limit our freedom to operate and prevent us from commercializing our technology in accordance with our plans.

The occurrence of any of these events could impair our ability to operate without infringing upon the proprietary rights of others or prevent us from establishing or maintaining a competitive advantage over our competitors.

Variability in intellectual property laws may adversely affect our intellectual property position.

Intellectual property laws, and patent laws and regulations in particular, have been subject to significant variability either through administrative or legislative changes to such laws or regulations or changes or differences in judicial interpretation, and it is expected that such variability will continue to occur. Additionally, intellectual property laws and regulations differ by country. Variations in the patent laws and regulations or in interpretations of patent laws and regulations in the United States and other countries may diminish the value of our intellectual property and may change the impact of third-party intellectual property on us. Accordingly, we cannot predict the scope of the patents that may be granted to us with certainty, the extent to which we will be able to enforce our patents against third parties or the extent to which third parties may be able to enforce their patents against us.

Some of the intellectual property that is important to our business is owned by other companies or institutions and licensed to us, and changes to the rights we have licensed may adversely impact our business.

We license from third parties some of the intellectual property that is important to our business. If we fail to meet our obligations under these licenses, these third parties could terminate the licenses. If the third parties who license intellectual property to us fail to maintain the intellectual property that we have licensed, or lose rights to that intellectual property, the rights we have licensed may be reduced or eliminated, which could subject us to claims of intellectual property infringement. Termination of these licenses or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms, or could subject us to claims of intellectual property infringement in litigation or other administrative proceedings that could result in damage awards against us and injunctions that could prohibit us from selling our products. In addition, some of our licenses from third parties limit the field in which we can use the licensed technology. Therefore, in order for us to use such licensed technology in potential future applications that are outside the licensed field of use, we may be required to negotiate new licenses with our licensors or expand our rights under our existing licenses. We cannot assure you that we will be able to obtain such licenses or expanded rights on reasonable terms or at all. In addition, we have limited rights to participate in the prosecution and enforcement of the patents and patent applications that we have licensed. As a result, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. Further, because of the rapid pace of technological change in our industry, we may need to rely on key technologies developed or licensed by third parties, and we may not be able to obtain licenses and technologies from these third parties at all or on reasonable terms. The occurrence of these events may have a material adverse effect on our business, financial condition or results of operations.

The measures that we use to protect the security of our intellectual property and other proprietary rights may not be adequate, which could result in the loss of legal protection for, and thereby diminish the value of, such intellectual property and other rights.

In addition to patents, we also rely upon trademarks, trade secrets, copyrights and unfair competition laws, as well as license agreements and other contractual provisions, to protect our intellectual property and other proprietary rights. Despite these measures, any of our intellectual property rights could be challenged, invalidated, circumvented or misappropriated. In addition, we attempt to protect our intellectual property and proprietary information by requiring our employees and consultants to enter into confidentiality and assignment of inventions agreements, and by entering into confidentiality agreements with our third-party development, manufacturing, sales and distribution partners, who may also acquire, develop and/or commercialize alternative or competing products or provide services to our competitors. For example, Roche has had certain access to our trade secrets and other proprietary information pursuant to a development agreement that we had with Roche, subject to the confidentiality provisions thereof; however, Roche has also developed and commercialized its 454 Life Sciences sequencing systems and is developing alternative and potentially competing sequencing products through its acquisition of Genia Technologies. There can be no assurance that our measures will provide adequate protection for our intellectual property and proprietary information. These agreements may be breached, and we may not have adequate remedies for any such breach. In addition, our trade secrets and other proprietary information may be disclosed to others, or others may gain access to or disclose our trade secrets and other proprietary information. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming, and the outcome is unpredictable. Additionally, others may independently develop proprietary information and techniques that are substantially equivalent to ours. The occurrence of these events may have a material adverse effect on our business, financial condition or results of operations.

Our intellectual property may be subject to challenges in the United States or foreign jurisdictions that could adversely affect our intellectual property position.

Our pending, issued and granted U.S. and foreign patents and patent applications have been, are and may in the future be, subject to challenges by third parties asserting prior invention by others or invalidity on various grounds, through proceedings, such as interferences, reexamination or opposition proceedings. Addressing these challenges to our intellectual property has been, and any future challenges can be, costly and distract management’s attention and resources. For example, we previously incurred significant legal expenses to litigate and settle a complaint seeking review of a patent interference decision of the U.S. Patent and Trademark Office. Additionally, as a result of these challenges, our patents or pending patent applications may be determined to be unpatentable to us, invalidated or unenforceable in whole or in part. Accordingly, adverse rulings in these proceedings may negatively impact the scope of our intellectual property protection for our products and technology, and may materially and adversely affect our business.

Some of our technology is subject to “march-in” rights by the U.S. government.

Some of our patented technology was developed with U.S. federal government funding. When new technologies are developed with U.S. government funding, the government obtains certain rights in any resulting patents, including a nonexclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise “march-in” rights to use or allow third parties to use our patented technology. The government can exercise its march-in rights if it determines that such action is necessary to (i) achieve practical application of the U.S. government-funded technology, (ii) alleviate health or safety needs, (iii) meet requirements of federal regulations, or (iv) give preference to U.S. industry. In addition, U.S. government-funded inventions must be reported to the government and such government funding must be disclosed in any resulting patent applications. Furthermore, our rights in such inventions are subject to government license rights and foreign manufacturing restrictions.

We are involved in legal proceedings to enforce our intellectual property rights.

Our intellectual property rights involve complex factual, scientific and legal questions. We operate in an industry characterized by significant intellectual property litigation. Even though we may believe that we have a valid patent on a particular technology, other companies may have from time to time taken, and may in the future take, actions that we believe violate our patent rights. For example, we have filed a complaint with the U.S. International Trade Commission against Oxford Nanopore Technologies Ltd. for patent infringement. Legal actions to enforce our patent rights can be expensive and may involve the diversion of significant management time and resources and adverse parties may bring claims against us and/or our intellectual property. Our enforcement actions may not be successful, could give rise to legal claims against us and could result in some of our intellectual property rights being determined to be invalid or not enforceable.

We could in the future be subject to legal proceedings with third parties who may claim that our products infringe or misappropriate their intellectual property rights.

Our products are based on complex, rapidly developing technologies. We may not be aware of issued or previously filed patent applications that belong to third parties that mature into issued patents that cover some aspect of our products or their use. In addition, because patent litigation is complex and the outcome inherently uncertain, our belief that our products do not infringe third-party patents of which we are aware or that such third-party patents are invalid and unenforceable may be determined to be incorrect. As a result, third parties have claimed, and may in the future claim, that we infringe their patent rights and have filed, and may in the future file, lawsuits or engage in other proceedings against us to enforce their patent rights. In addition, as we enter new markets, our competitors and other third parties may claim that our products infringe their intellectual property rights as part of a business strategy to impede our successful entry into those markets. Furthermore, parties making claims against us may be able to obtain injunctive or other relief, which effectively could block our ability to develop further, commercialize, or sell products or services, and could result in the award of substantial damages against us. Patent litigation between competitors in our industry is common. Additionally, we have certain obligations to many of our customers and suppliers to indemnify and defend them against claims by third parties that our products or their use infringe any intellectual property of these third parties. In defending ourselves against any of these claims, we have in the past incurred, and could in the future incur, substantial costs, and the attention of our management and technical personnel could be diverted. For example, we previously incurred significant legal expenses to litigate and settle a complaint alleging patent infringement. Even if we have an agreement that indemnifies us against such costs, the indemnifying party may be unable to uphold its contractual obligations. To avoid or settle legal claims, it may be necessary or desirable in the future to obtain licenses relating to one or more products or relating to current or future technologies, which could negatively affect our gross margins. We may not be able to obtain these licenses on commercially reasonable terms, or at all. We may be unable to modify our products so that they do not infringe the intellectual property rights of third parties. In some situations, the results of litigation or settlement of claims may require us to cease allegedly infringing activities which could prevent us from selling some or all of our products. The occurrence of these events may have a material adverse effect on our business, financial condition or results of operations.

In addition, in the course of our business, we may from time to time have access or be alleged to have access to confidential or proprietary information of others, which, though not patented, may be protected as trade secrets. Others could bring claims against us asserting that we improperly used their confidential or proprietary information, or that we misappropriated their technologies and incorporated those technologies into our products. A determination that we illegally used the confidential or proprietary information or misappropriated technologies of others in our products could result in us paying substantial damage awards or being prevented from selling some or all of our products, which could materially and adversely affect our business.

We have not yet registered some of our trademarks in all of our potential markets, and failure to secure those registrations could adversely affect our business.

Some of our trademark applications may not be allowed for registration, and our registered trademarks may not be maintained or enforced. In addition, in the U.S. Patent and Trademark Office and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings.

Our use of “open source” software could adversely affect our ability to sell our products and subject us to possible litigation.

A portion of our products or technologies developed and/or distributed by us incorporate “open source” software, and we may incorporate open source software into other products or technologies in the future. Some open source software licenses require that we disclose the source code for any modifications to such open source software that we make and distribute to one or more third parties, and that we license the source code for such modifications to third parties, including our competitors, at no cost. We monitor the use of open source software in our products to avoid uses in a manner that would require us to disclose or grant licenses under our source code that we wish to maintain as proprietary; however, there can be no assurance that such efforts have been or will be successful. In some circumstances, distribution of our software that includes or is linked with open source software could require that we disclose and license some or all of our proprietary source code in that software, which could include permitting the use of such software and source code at no cost to the user. Open source license terms are often ambiguous and there is little legal precedent governing the interpretation of these licenses. Successful claims made by the licensors of open source software that we have violated the terms of these licenses could result in unanticipated obligations, including being subject to significant damages, being enjoined from distributing products that incorporate open source software and being required to make available our

proprietary source code pursuant to an open source license, which could substantially help our competitors develop products that are similar to or better than ours or otherwise materially and adversely affect our business.

Risks Related to Owning Our Common Stock

The price of our common stock has been, is, and may continue to be, highly volatile, and you may be unable to sell your shares at or above the price you paid to acquire them.

The market price of our common stock is highly volatile, and we expect it to continue to be volatile for the foreseeable future in response to many risk factors listed in this section, and others beyond our control, including:

- actual or anticipated fluctuations in our financial condition and operating results;
- announcements of technological innovations by us or our competitors;
- announcements by our customers, partners or suppliers relating directly or indirectly to our products, services or technologies;
- 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, capital commitments or achievement of significant milestones;
- 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 or 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;
- stock price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- reports, guidance and ratings issued by securities or industry analysts; and
- general economic and market conditions.

If any of the forgoing occurs, it would cause our stock price or trading volume to decline. Stock markets in general and the market for companies in our industry in particular have experienced price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These broad market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations, may negatively impact the market price of our common stock. You may not realize any return on your investment in us and may lose some or all of your investment. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We have been a party to this type of litigation in the past and may be the target of this type of litigation again in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Future sales of our common stock could cause our stock price to fall.

We maintain a shelf registration statement on Form S-3 with the SEC pursuant to which we may, from time to time, sell up to an aggregate of $150 million of our common stock, preferred stock, depositary shares, warrants, units or debt securities. We have established, and may in the future establish, "at-the-market" offering programs pursuant to which we may offer and sell shares of our common stock. In February 2017, we intend to file an additional prospectus supplement pursuant to which we may offer and sell, from time to time, additional shares of our common stock having an aggregate offering price of up to $60.0 million under an "at-the-market" offering program. Sales of securities under the registration statement have resulted and will continue to result in dilution of our existing stockholders, and such sales could cause our stock price to fall.

In addition, if our existing stockholders sell, or indicate an intent to sell, a large number of shares of our common stock in the public market, it could cause our stock price to fall. We may also issue shares of common stock or securities convertible into our common stock from time to time in connection with financings, acquisitions, investments or otherwise. Any such issuance would result in dilution to our existing stockholders and could cause our stock price to fall.

Concentration of ownership by our principal stockholders may result in control by such stockholders of the composition of our board of directors.

Our existing significant stockholders, executive officers, directors and their affiliates beneficially own a significant number of our outstanding shares of common stock. As a result, these stockholders will be able to exercise a significant level of control over all matters

requiring stockholder approval, including the election of directors. This control could have the effect of delaying or preventing a change of control of our company or changes in management and will make the approval of certain transactions difficult or impossible without the support of these stockholders.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management and limit the market price of our common stock.

Provisions in our certificate of incorporation and bylaws, as amended and restated, may have the effect of delaying or preventing a change of control or changes in our management. Our amended and restated certificate of incorporation and bylaws include provisions that:

- authorize our board of directors to issue, without further action by the stockholders, up to 50,000,000 shares of undesignated preferred stock and up to approximately 1,000,000,000 shares of authorized but unissued shares of common stock;
- require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;
- specify that special meetings of our stockholders can be called only by our board of directors, the Chairman of the Board, the Chief Executive Officer or the President;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered terms;
- provide that our directors may be removed only for cause; and
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Our large number of authorized but unissued shares of common stock may potentially dilute existing stockholders' stockholdings.

We have a significant number of authorized but unissued shares of common stock. Our board of directors may issue shares of common stock from this authorized but unissued pool from time to time without stockholder approval, resulting in the dilution of our existing stockholders.

We do not intend to pay dividends for the foreseeable future.

We have never declared or paid any dividends on our common stock and do not intend to pay any dividends in the foreseeable future. In addition, the terms of our existing debt agreement restrict our ability to pay dividends on our common stock. We anticipate that we will retain all of our future earnings for use in the operation of our business and for general corporate purposes. Any determination to pay dividends in the future will be at the discretion of our board of directors. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investments.