Pacific Biosciences (PACB)/Illumina (ILMN)

AGREED MERGER

Deal Terms

1 PACB = $8.00

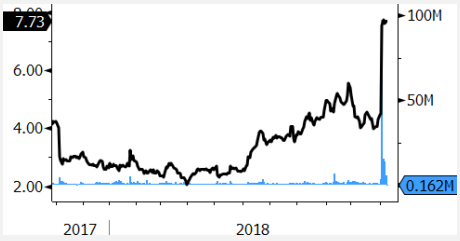
Target: Pacific Biosciences of California

Country	United States
Bloomberg	PACB US
Sector	Life Science Equipment
Share price ($)	7.69
Market cap ($m)	1,131
Free float (%)	~93

Acquirer: Illumina

Country	United States
Bloomberg	ILMN
Sector	Life Science Equipment
Share price ($)	321.48
Market cap ($m)	47,869
Free float (%)	~100

Price Chart



Status

HSR filing deadline - November 26, 2018

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The deal spread appears to be somewhat tight.

Given the lengthy deal timeline, the antitrust risk, the upside and downside scenarios we believe that the current spread of 2.5% does not offer a favorable risk/reward.

Key risks

Regulatory Risks and Timing

- It appears that the key risk is antitrust approval (most likely only US, potentially EU, China unlikely) and therefore the potentially lengthy deal timeline.
- Both companies provide gene sequencing solutions. However, PACB serves the long-read while ILMN serves the short-read market.
- Illumina is the biggest manufacturer of gene sequencing machines and consumables used in gene sequencing. Its machines have been used to perform 90% of all sequencing done to date.
- PacBio is a niche player in the long-read space.
- Illumina estimates that the total addressable market for long-read applications was $660 million last year, and that it could grow at a 30% compound annual rate to $2.5 billion in 2022. PACB's 2017 revenue was $93.5m with a 14% market share in long read market. Other long read players with 25%-30% market share are Helicos, Oxford Nanopore and Complete Genomics (BGI of China).

The key questions are:

- is there substitutability between the two methods;
- and the potential foreclosure of competitors via bundling. Given that the two methods are also used combined, ILMN might foreclose competitors via bundling.
- The sequencing read length depends on the instrument and chemistry used. The range of the read length of a short-read sequencing instrument is between 100 and 600 bp, while that of a long-read sequencing instrument varies between 10 to 15 kb. The choice one makes depends on the goal of the experiment; one isn't considered universally superior to the other.

Substitutability

- Based on industry related publications it appears there is no substitutability between the two methods therefore the long and short methods are likely to be considered as distinct product markets by regulators. Thus, the significant market share of ILMN and the incremental addition of PACB – which could cause problem if a single market would be defined for the two methods – is unlikely to be an issue.

Bundling

- As per our reading of the industry practice the best result can be achieved via the combination of the two methods.
- In our view there is substantial risk that ILMN will bundle its two products and so it will be able to foreclose competitors which would further increase its 80%+ market share.
- Consequently, we believe that antitrust authorities might conduct investigation whether the merger could create possibilities for exclusionary bundling or tying practices that could possibly foreclose competitors and decrease competition in the concerned markets:
- In our view, it might be difficult to structure any remedies that would prevent companies from bundling products post-transaction.
- However, we believe that regulators will definitely seek commitment to assure that smaller players are not left out of the competition (post-transaction).
- We note that customers' - research institutions, commercial laboratories, genome centers, clinical, government and academic institutions, genomics service providers, pharmaceutical companies and agricultural companies – bargaining power might mitigate the bundling issue.
- In case of PACB/ILMN transaction, we may see similarity to the GE/Honeywell case: there is effectively no firm that is able to compete with bundled products; and consequently, it might result in further market share increase for ILMN.
- Also, we believe that the already high market concentration increases potential tying concerns.
- We believe that an HSR second request highly likely and estimate a 5-7 months antitrust timeline.

Shareholder Vote

- Given the generous premium we believe (in lack of a counterbid) shareholder support is unlikely to be an issue.

Counterbid

- A counterbid is possible from Thermo Fisher, Agilent, Qiagen or Roche.

Key terms of the merger

Transaction Details	
Announcement Date	**November 1, 2018**
Offer terms	1 PACB = $8.00
% owned by PACB stockholders	0%
Deal Size (Market Value)	$1,191m
Offer structure	All cash merger
Target's Board Recommendation	Yes
Voting Agreement	Yes ■ In connection with the execution of the Merger Agreement, each of Bill Ericson, Christian Henry, David Botstein, John Milligan, Kathy Ordonez, Lucy Shapiro, Marshall Mohr, Michael Hunkapiller, Michael Phillips, Randall Livingston, and Susan Barnes (collectively, the "Company Stockholders") have entered into a Voting Agreement. Subject to the terms and conditions of the Voting Agreement, the Company Stockholders have agreed, among other things, to vote the shares of PacBio common stock that are owned of record by such stockholder (**representing in the aggregate approximately 1.98% of the total outstanding shares of Company common stock as of October 30, 2018**), and including shares of Company Common Stock acquired after such date, in favor of the adoption of the Merger Agreement and approval of the Merger and to waive any applicable appraisal rights. In addition, each such stockholder has agreed to **vote against any proposal made in competition with the Merger**, as well as certain other restrictions with respect to the voting and transfer of such stockholder's shares of Company common stock.
Target Incorporation	Delaware (US)
Merger Agreement	Click here for the merger agreement
Merger Call	Click here for the merger call
Synergies	■ Hasn't been mentioned ■ CBR est: ~30% of SGA $20m p/a

Indicated Closing Date

- The deal isn't expected to close until the middle of next year

Dividends

- PACB cannot pay dividend.

Financing

- The transaction is not subject to any financing condition.

PACB capitalization

- **PACB Equity**
  - As of 5:00 p.m., Pacific time, on October 30, 2018 (such date and time, the "Capitalization Date"), there were outstanding (A) 148,901,892 shares of Common Stock, (B) no shares of Preferred Stock, (C) 38,835,378 shares of Common Stock reserved under the Employee Plans (excluding shares of Common Stock subject to issuance under the ESPP), of which there were outstanding 26,930,553 shares of Common Stock subject to issuance upon exercise of outstanding Company Stock Options (which have a weighted average exercise price of $5.5892 and 18,861,777 of which are currently exercisable), (D) 957,181 shares of Common Stock subject to issuance upon settlement of Company RSUs, and (E) 1,952,507 shares of Common Stock reserved for issuance under the ESPP.
- **PACB Debt**
  - 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

	Payments due by period (in thousands)						
	Total	2018	2019	2020	2021	2022	After
Operating lease obligations (1)	$ 74,790	$ 6,822	$ 6,930	$ 7,056	$ 7,272	$ 7,488	$ 39,222
Debt (2)	19,291	1,400	1,400	16,491	—	—	—
Total contractual obligations	$ 94,081	$ 8,222	$ 8,330	$ 23,547	$ 7,272	$ 7,488	$ 39,222

(1) Maintenance, insurance, taxes and contingent rent obligations are excluded.
(2) Amounts in the table above include interest and principal repayments on the debt.

Valuation Multiples

- **1-day premium** 71%
- **LTM EV/Sales** 13.0x
- **FY1 EV/Sales** 13.1x
- **FY2 EV/Sales** 9.5x
- **LTM P/Sales** 14.2x
- **FY1 P/ Sales** 14.4x
- **FY2 P/Sales** 10.4x

Timetable

- **Confidentiality Agreement** September 11, 2018
- **Date of the Merger Agreement (T)** November 1, 2018
- **Deal Announcement** November 1, 2018
- **HSR filing deadline (15 BD)** November 26, 2018
- **Proxy filing** By mid-December 2018
- **Expiration of initial HSR waiting period (+30D)** By December 26, 2018
- **Definitive Proxy** By end of January 2019
- **PACB shareholder meeting** By early March 2019
- **Regulatory approvals in place** By mid-2019
- **Settlement (CBR est.)** By mid-2019
- **Outside date** November 1, 2019

Deal close definition

- Subject to the provisions of Article 9 the closing of the Merger (the "Closing") shall take place in Palo Alto, California at the offices of Covington & Burling LLP, 5 Palo Alto Square, 10th Floor, Palo Alto, CA 94306-2112 as soon as possible, but in any event no later than three Business Days after the date the conditions set forth in Article 9 (other than conditions that by their nature are to be satisfied at the Closing, but subject to the satisfaction or, to the extent permissible, waiver of those conditions at the Closing) have been satisfied or, to the extent permissible, waived by the party or parties entitled to the benefit of such conditions, or at such other place or time as Parent and the Company may mutually agree. The date on which the Closing occurs is referred to in this Agreement as the "Closing Date."

Solicitation Clause (PACB)

- There is a non-solicitation clause with a fiduciary out prior to the PACB shareholder vote
- There is a four-business day matching period (might be reduced to two)

"Superior Proposal"

- means a bona fide, written Acquisition Proposal that was not solicited in breach of this Section 6.04 (with all percentages in the definition of Acquisition Proposal deemed to refer to 50%) on terms that the Board of Directors (or a committee thereof) determines, in good faith, after consultation with a financial advisor and outside legal counsel, are more favorable from a financial point of view to the Company's stockholders than as provided hereunder (taking into account any revisions proposed by Parent to amend the terms of this Agreement pursuant to Section 6.04(d) or otherwise at the time of such determination and after taking into account those factors and matters deemed relevant in good faith by the Board of Directors (or a committee thereof), including the identity of the Person making the proposal, the likelihood of consummation in accordance with the terms of such proposal and the legal, financial (including the financing terms), regulatory, timing and other aspects of such proposal).

Company Intervening Event

- The Board of Directors (or a committee thereof) may make an Adverse Recommendation Change in response to any positive material change, effect, development, circumstance, condition, event or occurrence that as of the date of this Agreement was not known to the Board of Directors, or the consequences of which (based on facts known to the Board of Directors as of the date of this Agreement) were not reasonably foreseeable as of the date of this Agreement (an "Intervening Event");
- provided that in no event shall any of the following constitute or contribute to an Intervening Event:
  - (A) changes in the financial or securities markets or general economic, political or business conditions in the United States or other jurisdictions in which the Company or any of its Subsidiaries has operations,
  - (B) changes (including changes of Applicable Law) or conditions generally affecting the industry in which the Company and its Subsidiaries operate,
  - (C) changes in GAAP or other applicable accounting rules or

- (D) the receipt, existence or terms of any Acquisition Proposal or any inquiry, offer, request or proposal that would reasonably be expected to lead to an Acquisition Proposal;

Key conditions to the merger	
Shareholder approvals	PACB - the affirmative vote of the holders of a majority of the outstanding Shares
Regulatory Approvals	Yes - HSR
No injunctions	Yes
No legal prohibition	Yes
Reps and warranties	Yes
Covenants fulfilled	Yes
No Company MAC	Yes
Closing Certificate	Yes

MAC Definition

- **"Parent Material Adverse Effect"** means a material adverse effect on Parent's ability to consummate the transactions contemplated by this Agreement.
- **"Company Material Adverse Effect"** means any event, circumstance, change, occurrence, development, condition or effect that, individually or in the aggregate, has or would reasonably be expected to result in a material adverse change in, or material adverse effect on, the financial condition, business, assets, liabilities or results of operations of the Company and its Subsidiaries, taken as a whole.

PACB MAC Carve-outs

- Excluding any such effect to the extent resulting from
- (i) changes in general economic conditions in the United States or global credit, currency, financial or capital markets,
- (ii) changes in United States or global regulatory, legal, legislative or political conditions (including changes or proposed changes in Applicable Law or GAAP),
- (iii) changes or conditions generally affecting the industry in which the Company and its Subsidiaries operate,
- (iv) geopolitical conditions, acts of war, sabotage or terrorism, outbreak or escalation of hostilities or war or epidemics, pandemics or natural disasters,
- (v) the announcement or pendency of the transactions contemplated by this Agreement, including the impact thereof on relationships of the Company or its Subsidiaries, contractual or otherwise, with customers, suppliers, distributors, partners, employees or regulators, it being understood that termination, change of control and other similar rights of Third Parties that are required to be disclosed in the Company Disclosure Schedule will not be deemed to be events, circumstances, changes, occurrences, developments, conditions or effects related to the announcement or pendency of the transactions contemplated by this Agreement for purposes of the references to Company Material Adverse Effect in this Agreement,
- (vi) any decline, in and of itself, in the market price, or change in trading volume, of any capital stock of the Company (it being understood that any cause of such decline or change may be taken into consideration when determining whether a Company Material Adverse Effect has occurred),
- (vii) any failure, in and of itself, of the Company to meet any internal or public projections, forecasts, budgets or estimates of revenue, earnings, cash flow or cash position Company (it being understood that any cause of such failure may be taken into consideration when determining whether a Company Material Adverse Effect has occurred), or
- (viii) any action taken by the Company that is expressly required by this Agreement or taken at the prior written request of or with the prior written consent of Parent
- except, in the case of clauses **(i), (ii), (iii) and (iv), to the extent not having a disproportionate effect** on the Company and its Subsidiaries, taken as a whole, relative to other participants in the industry in which the Company and its Subsidiaries operate (in which case on the only incremental disproportionate adverse impact may be taken into account).

Break fees	
Break fee	\$43m (\$0.29/PACB) Specifically, if the Merger Agreement is terminated in connection with PacBio accepting a superior offer or due to the withdrawal by PacBio's board of directors of its recommendation of the Merger, If (A) this Agreement is terminated by Parent pursuant to Section 10.01(c)(ii) or by either Parent or the Company pursuant to Section 10.01(b)(ii), (B) after the date of this Agreement and prior to such termination, an Acquisition Proposal shall have been publicly announced or otherwise communicated to the Company, the Board of Directors or the Company's stockholders (provided that in the case of a termination pursuant to Section 10.01(c)(ii)(A), all percentages in the definition of Acquisition Proposal will be deemed to refer to 50%), and (C) within 12 months following the date of such termination, the Company or any of its Subsidiaries shall have entered into a definitive agreement with respect to an Acquisition Proposal or an Acquisition Proposal shall have been consummated (provided that for purposes of this clause (C), all percentages in the definition of Acquisition Proposal will be deemed to refer to 50%), then the Company shall pay (or cause to be paid) to Parent in immediately available funds, prior to or concurrently with the occurrence of the applicable event described in clause (C), the Company Termination Fee.
Reverse break fee	\$98m (\$0.66/PACB) If this Agreement is terminated by Parent or the Company pursuant to Section 10.01(b)(i) and at the time of such termination, all of the conditions set forth in Section 9.01 and Section 9.02 shall have been satisfied or validly waived (other than one or both of (x) Section 9.01(b), Section 9.01(c) or Section 9.02(vii) (but, with respect to Section 9.01(c) and Section 9.02(vii), only if the applicable

Legal Restraint or Applicable Law relates to an Antitrust Law; provided, that if there is additionally a failure to satisfy or waive any of Section 9.01(b), Section 9.01(c) or Section 9.02(vii) due to a Legal Restraint or Applicable Law relating to a Specified Jurisdiction, this subsection (x) shall nonetheless be satisfied) and (y) those conditions that by their nature are to be satisfied at the Closing, provided that such conditions were then capable of being satisfied if the Closing had occurred on the date of such termination), then Parent shall pay to the Company in immediately available funds $98,000,000 (the "Reverse Termination Fee") within two Business Days after such termination.

Antitrust related clauses

Jurisdictions	US
Divestiture obligation	Yes (PACB assets only)
Litigation obligation	No
Reverse break fee (regulatory)	Yes – $98m

Specific Performance

Yes

Governing Law

State of Delaware

Key PACB shareholders

Shareholders	%
Consonance Capital Management LP	8.5
Maverick Capital Ltd	8.2
Orade Investment Management Inc	6.5
BlackRock Inc	6.5
Capital Group Cos Inc/The	6.3
ARK Investment Management LLC	5.2
Vanguard Group Inc/The	4.0
MDV Management Co LLC	3.4
ArrowMark Colorado Holdings LLC	3.0
Point72 Asset Management LP/Old	2.0
Others	**46.5**

Source: Bloomberg

Company descriptions & rationale for the merger

PACB DESCRIPTION

- PACB designs, develops and manufactures sequencing systems to help scientists resolve genetically complex problems. Based on the novel Single Molecule, Real-Time (SMRT®) sequencing technology, PACB's 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. Its technology provides high accuracy, ultra-long reads, uniform coverage and 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.

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 N4-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, N6-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 the 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

- PACB has developed its 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, PACB offers and supports 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, PACB utilizes its nanoscale innovation, the zero-mode waveguide, or ZMW.
- The ZMWs in the 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. The 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, the immobilization process randomly distributes polymerases into ZMWs across the SMRT Cell, typically resulting in approximately one-third to two-thirds of the ZMWs having a single template.

Phospholinked Nucleotides

- The 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. PACB no longer manufactures the PacBio RS II instrument; however, it continues to service and support installed PacBio RS II instruments. 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 the 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. In addition, SMRT sequencing can achieve high accuracy when sequencing through complex and highly repetitive regions, whereas other sequencing methods are unable to resolve such regions, which can often result in poor accuracy.
- 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
  - The 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.

Customers

- Customers include research institutions, commercial laboratories, genome centers, clinical, government and academic institutions, genomics service providers, pharmaceutical companies and agricultural companies. In general, the customers will isolate, prepare and analyze genetic samples using PacBio sequencing systems in their own research labs, or they will send their genetic samples to third party service providers who in turn will sequence the samples with PacBio systems and provide the sequence data back to the customer for further analysis. 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. Excluding contractual revenue from the Development, Commercialization and License Agreement dated September 24, 2013 (the "Roche Agreement") with F. Hoffman-La Roche Ltd ("Roche"), which has now been terminated, for the year ended December 31, 2017, one customer, Gene Company Limited, accounted for approximately 31% of its total revenue, and for the years ended December 31, 2016 and 2015, no customer accounted for more than 10% of the total revenue.
- PACB believes that the majority of the current customers are early adopters of sequencing technology. By focusing the efforts on high-value applications, and developing whole product solutions around these applications, PACB seeks to drive the adoption of its 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.
- PACB currently sells its products to a number of customers outside the United States, including customers in other areas of North America, Europe, Asia Pacific (including the Middle East). Roche related contractual revenue has been classified as revenue from the United States. Revenue from customers outside the United States totaled $54.3 million, or 58% of the total revenue during fiscal 2017, compared to $41.0 million, or 45% of the total revenue, during fiscal 2016, and compared to $24.9 million, or 27% of the total revenue, during fiscal 2015.

Segment and Geographic Information

- PACB is organized as, and operate in, one reportable segment. The total revenue was $93.5 million for the year ended December 31, 2017. The operating loss was $89.8 million for the year ended December 31, 2017. The total assets were $144.1 million as of December 31, 2017.

Revenue by geographic

$m	FY 2017	% of total
North America	41	43.4%
Asia Pacific(including the middle east)	40	42.5%
Europe	13	14.1%
Total	**94**	**100.0%**

Source: Bloomberg, CBR

Intellectual Property

- The 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 PACB owns, as well as some of the patents and applications that it has licensed from other parties, are subject to U.S. government march-in rights, whereby the U.S. government may disregard the exclusive patent rights on its own behalf or on behalf of third parties by imposing licenses in certain circumstances, such as if PACB fails 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, 2017, PACB owns or holds exclusive licenses to 267 issued U.S. patents, 89 pending U.S. patent applications, 183 granted foreign patents and 78 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 2036. PACB also has non-exclusive patent licenses with various third parties to supplement its own large and robust patent portfolio.

- Of its exclusively licensed patent applications, 22 issued U.S. patents, one pending U.S. patent application, and 15 granted foreign patents are licensed to us by the Cornell Research Foundation, which manages technology transfers on behalf of Cornell University. PACB has 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. PACB 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.
- PACB is involved in several legal proceedings for patent infringement with Oxford Nanopore Technologies Ltd., Oxford Nanopore Technologies, Inc., Metrichor, Ltd. and Harvard University in several United States and European jurisdictions.

Competition

- 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 PACB does. They also have larger and more established manufacturing capabilities and marketing, sales and support functions. PACB expects 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 the sales, profitability or market share.
- In order for PACB to successfully compete against these companies, it will need to demonstrate that its products deliver superior performance and value as a result of the 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.

ILMN DESCRIPTION

- ILMN is the global leader in sequencing- and array-based solutions for genetic analysis. The products and services serve customers in a wide range of markets, enabling the adoption of genomic solutions in research and clinical settings.
- The customers include leading genomic research centers, academic institutions, government laboratories, and hospitals, as well as pharmaceutical, biotechnology, commercial molecular diagnostic laboratories, and consumer genomics companies.
- The portfolio of integrated sequencing and microarray systems, consumables, and analysis tools is designed to accelerate and simplify genetic analysis. This portfolio addresses the range of genomic complexity, price points, and throughput, enabling customers to select the best solution for their research or clinical challenge.
- ILMN has also enabled, or invested in, early-stage companies that are pursuing promising genomics-related technologies. For example, GRAIL, Inc. (GRAIL), formed in 2016, was created to develop a blood test for early-stage cancer detection; and Helix Holdings I, LLC (Helix) was established in 2015 to enable individuals to explore their genetic information by providing sequencing and services for consumers through third-party partners. Helix is a consolidated variable interest entity (VIE), and GRAIL was deconsolidated in February 2017.

Principal Markets

The organization is structured to target the markets and customers outlined below.

Life Sciences

- Historically, the core business has been in the life sciences research market. This includes laboratories associated with universities, research centers, and government institutions, along with biotechnology and pharmaceutical companies. Researchers at these institutions use ILMN products and services for basic and translational research across a spectrum of scientific applications, including targeted, exome, and whole-genome sequencing; genetic variation; gene expression; epigenetics; and metagenomics. Next-generation sequencing (NGS) technologies are being adopted due to their declining costs per sample and their ability to sequence large sample sizes quickly and accurately, generating vast amounts of high-quality data. Both private and public funding drive this research, along with global initiatives to characterize genetic variation.
- ILMN's products also serve various applied markets including consumer genomics and agrigenomics. For example, in consumer genomics, customers use ILMN's technologies to provide personalized genetic data and analysis to individual consumers. In agrigenomics, government and corporate researchers use ILMN products and services to explore the genetic and biological basis for productivity and nutritional constitution in crops and livestock. Researchers can identify natural and novel genomic variation and deploy genome-wide marker-based applications to accelerate breeding and production of healthier and higher-yielding crops and livestock.

Clinical Genomics

- ILMN is focused on enabling translational and clinical markets through the introduction of best-in-class sequencing instruments and reagents. Further, ILMN is developing sample-to-answer solutions to catalyze adoption in the clinical setting, including in reproductive and genetic health and oncology. In reproductive health, ILMN's primary focus is driving noninvasive prenatal testing (NIPT) adoption globally through its technology, which identifies fetal chromosomal abnormalities by analyzing cell-free DNA in maternal blood. The NGS technology is also accelerating rare and undiagnosed disease research to discover the genetic causes of inherited disorders by assessing many genes simultaneously. Using NGS can reduce costs compared to traditional methods of disease diagnosis, which are often expensive and inconclusive while requiring extensive testing.

- Cancer is a disease of the genome, and the goal of cancer genomics is to identify genomic changes that transform a normal cell into a cancerous one. Understanding these genomic changes will improve diagnostic accuracy, increase understanding of the prognosis, and enable oncologists to target therapies to individuals. Customers in the translational and clinical oncology markets use ILMN products to perform research that may help identify individuals who are genetically predisposed to cancer. Customers also utilize ILMN's technology to identify the molecular changes in a tumor so that physicians can tailor treatment based on the genetic variation. ILMN believes that circulating tumor DNA (ctDNA) will become an important clinical tool for managing oncology patients during all stages of tumor progression. The technology is being used to research the implications of ctDNA in treatment determination, treatment monitoring, minimal residual disease, and asymptomatic screening. For example, ILMN has invested in, and partnered with GRAIL, which ILMN formed to develop a blood-based test for early-stage cancer detection that is enabled by the sequencing technology.

Principal Products and Technologies

- The unique technology platforms support the scale of experimentation necessary for population-scale studies, genome-wide discovery, target selection, and validation studies. Customers use products to analyze the genome at all levels of complexity, from targeted panels to whole-genome sequencing. A large and dynamic Illumina user community has published tens of thousands of customer-authored scientific papers using its technologies. Through rapid innovation, ILMN is changing the economics of genetic research, enabling projects that were previously considered impossible, and supporting clinical advances towards precision medicine.
- Most of ILMN product sales consist of instruments and consumables (which include reagents, flow cells, and microarrays) based on its proprietary technologies. For the fiscal years ended December 31, 2017 instrument sales comprised 19% of total revenues, and consumable sales represented 64% of total revenues.

Illumina Platform Overview:

From genome-wide discovery to targeted validation and screening

	Sequencing						Sequencing & Arrays	Arrays
Instrument	NovaSeq™ 6000 System	HiSeq X™ Ten* System	HiSeq™ 4000 System	MiSeq™ and MiSeqDx™ ‡ Systems	MiniSeq™ System	iSeq™ 100 System	NextSeq™ 550 and NextSeq™ 550Dx‡ Systems	iScan™ System
Technologies	Sequencing by synthesis (SBS) powered by TruSeq™ Chemistry						SBS, TruSeq, BeadChip, Infinium™, Infinium XT	BeadArray, Infinium
Applications	Scalable throughput and flexibility for virtually any genome, sequencing method, and scale of project	Population- and production-scale whole-genome sequencing	Production-scale genome, exome, transcriptome sequencing, and more	MiSeq System—small genome, amplicon, targeted gene panel sequencing MiSeqDx System—FDA-cleared IVD system for CF screening and user-defined assays	Targeted DNA and RNA sequencing	Targeted, bacterial, and viral sequencing	NextSeq 550 System: Whole-genome sequencing, exome, transcriptome sequencing, and CNV analysis NextSeq 550Dx System: FDA cleared and CE-IVD system for NGS IVD assays and clinical research	SNP and whole-genome genotyping, CNV analysis, gene regulation, epigenetic analysis, gene expression analysis, and cytogenetic analysis

*The HiSeq X Ten System consists of 10 sequencing instruments.

For Research Use Only. Not for use in diagnostic procedures (except as specifically noted).
‡For In Vitro Diagnostic Use.

Sequencing

- DNA sequencing is the process of determining the order of nucleotide bases (A, C, G, or T) in a DNA sample. ILMN's portfolio of sequencing platforms represents a family of systems that ILMN believes set the standard for productivity, cost-effectiveness, and accuracy among NGS technologies. Customers use ILMN platforms to perform whole-genome, de novo, exome and RNA sequencing, and targeted resequencing of specific gene regions and genes.
- Whole-genome sequencing determines the complete DNA sequence of an organism. In de novo sequencing, the goal is to sequence and analyze a sample without using information from prior sequencing of that species. In targeted resequencing, a portion of the sequence of an organism is compared to a standard or reference sequence from previously sequenced samples to identify genetic variation. Understanding the similarities and differences in DNA sequence between and within species helps us understand the function of the structures encoded in the DNA.
- The DNA sequencing technology is based on ILMN's proprietary reversible terminator-based sequencing chemistry, referred to as sequencing by synthesis (SBS) biochemistry. SBS tracks the addition of labeled nucleotides as the DNA chain is copied in a massively parallel fashion. ILMN's SBS sequencing technology provides researchers with a broad range of applications and the ability to sequence even large mammalian genomes in a few days rather than weeks or years.
- The sequencing platforms can generate between 500 megabases (Mb) and 6.0 terabases (Tb) (equivalent to approximately 48 human genomes) of genomic data in a single run, depending on the instrument and application. There are different price points per gigabase (Gb) for each instrument, and for different applications, which range from small-genome, amplicon, and targeted gene-panel sequencing to population-scale whole human genome sequencing. Since ILMN launched its first sequencing system in 2007, its systems have reduced the cost of sequencing by more than a factor of 10,000. In addition, the sequencing time per Gb has dropped by a factor of approximately 12,000.

- The BaseSpace Informatics Suite cloud platform plays a critical role in supporting the sequencing applications. BaseSpace Suite integrates directly with ILMN's sequencing instruments, allowing customers to manage their biological sample and sequencing runs, process and analyze the raw genomic data, and derive meaningful results. It facilitates data sharing, provides data-storage solutions and streamlines analysis through a growing number of applications developed by us and the bioinformatics community.
- For the fiscal years ended December 31, 2017, January 1, 2017, and January 3, 2016, sequencing revenue comprised 83%, 84%, and 86%, respectively, of total revenues.

Arrays

- Arrays are used for a broad range of DNA and RNA analysis applications, including SNP genotyping, CNV analysis, gene expression analysis, and methylation analysis, and enable the detection of millions of known genetic markers on a single array.
- The BeadArray technology combines microscopic beads and a substrate in a proprietary manufacturing process to produce arrays that can perform many assays simultaneously. This facilitates large-scale analysis of genetic variation and biological function in a unique, high-throughput, cost-effective, and flexible manner. Using the BeadArray technology, ILMN achieves high-throughput analysis via a high density of test sites per array and the ability to format arrays in various configurations. To serve the needs of multiple markets and market segments, ILMN can vary the size, shape, and format of the substrate into which the beads self-assemble and create specific bead types for different applications. The iScan System and the NextSeq 550 System can be used to image arrays.
- For the fiscal years ended December 31, 2017, array revenue comprised 17% of total revenues.

Consumables

- ILMN has developed various library preparation and sequencing kits to simplify workflows and accelerate analysis. The sequencing applications include whole-genome sequencing kits, which sequence entire genomes of any size and complexity, and targeted resequencing kits, which can sequence exomes, specific genes, RNA or other genomic regions of interest. The sequencing kits maximize the ability of the customers to characterize the target genome accurately and are sold in various configurations, addressing a wide range of applications.
- Customers use Illumina array-based genotyping consumables for a wide range of analyses, including diverse species, disease-related mutations, and genetic characteristics associated with cancer. Customers can select from a range of human, animal, and agriculturally relevant genome panels or create their own custom arrays to investigate millions of genetic markers targeting any species.

Intellectual Property

- ILMN has an extensive intellectual property portfolio. As of February 1, 2018, ILMN owns or has exclusive licenses to 719 issued U.S. patents and 473 pending U.S. patent applications, including 32 allowed applications that have not yet issued as patents. The issued and pending patents cover various aspects of the arrays, assays, oligo synthesis, sequencing technology, instruments, digital microfluidics, software, bioinformatics, and chemical-detection technologies, and have terms that expire between 2018 and 2038. ILMN continues to file new patent applications to protect the full range of its technologies. ILM has filed or has been granted counterparts for many of these patents and applications in foreign countries.

Competition

- Although ILMN believe that its products and services provide significant advantages over products and services currently available from other sources, ILMN expects continued intense competition. Its competitors offer products and services for sequencing, SNP genotyping, gene expression, and molecular diagnostics markets. They include companies such as **Agilent Technologies, Inc., BGI, Oxford Nanopore Technologies Limited, Pacific Biosciences of California, Inc., QIAGEN N.V., Roche Holding AG., and Thermo Fisher Scientific, Inc.,** among others. Some of these companies have or will have substantially greater financial, technical, research, and other resources than ILMN does, along with larger, more established marketing, sales, distribution, and service organizations. In addition, they may have greater name recognition than ILMN does in the markets ILMN addresses, and in some cases a larger installed base of systems. ILMN expects new competitors to emerge and the intensity of competition to increase. To compete effectively, ILMN must scale its organization and infrastructure appropriately and demonstrate that its products have superior throughput, cost, and accuracy.

STRATEGIC RATIONALE FOR THE MERGER

- Historically, the challenge for long-read technologies has been accuracy and cost. However, Pacific Biosciences recent technology breakthroughs have demonstrated an unparalleled level of accuracy for native long reads, which - when coupled by the impending release of the company's 8M Smart Cell - will substantially improve the utility and affordability of this technology.
- "These innovations drive our enthusiasm for bringing our companies' technologies together now. Specifically:
    - PacBio's latest system update, released last month, including the version 3.0 chemistry and version 6.0 software, with new protocols, reagents, and algorithms doubled the previous output of the current Sequel system.
    - PacBio's recent demonstration of a unique workflow that generates the highest read accuracy of any long-read platform. With this level of accuracy, researchers will be able to create complete genome assemblies at Q50 consensus quality to

comprehensively and accurately detect all classes of variants. Importantly, PacBio's improved workflow will obviate the need for large quantities of high molecular weight DNA which hinders other long read technologies.

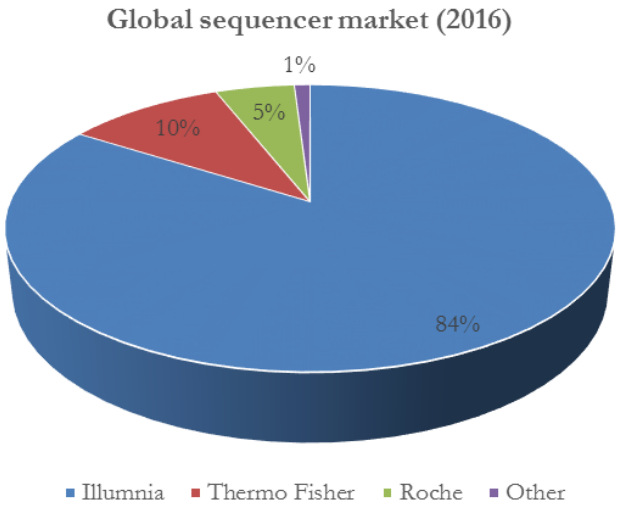
- These advances, coupled with the 8M Zero Mode Waveguide - or ZMW - chip expected to be available next year, will increase output and reduce cost per base of the Sequel system by an order of magnitude, enabling more economical and scalable approaches to discovery "

- PacBio's significant reduction in cost per Gb, improvement in accuracy, and faster turnaround time make long-read technologies accessible to a much larger user base. This is consistent with Illumina's long-standing commitment to democratize sequencing: enabling customers of all sizes to gain access to highly accurate sequencing technology with the broadest scope of applications.
- Bringing together Pacific Biosciences' highly accurate native long reads with Illumina's highly accurate and economical short reads, will uniquely position us to broaden and accelerate the use of sequencing across broad range of existing and emerging applications and move closer to delivering a perfect view of the genome: one that is accurate, complete, fast, and economical.
- "We are therefore very excited about the opportunity to combine with Pacific Biosciences for several strategic reasons:
  - First, we expect the combination will expand our addressable market by broadening the opportunities in de novo assembly in plant and animal, functional genomics, tissue transplant, and pharmacogenomics. These applications often require uniform, unbiased coverage in highly repetitive regions, which long-reads are best suited to provide. We believe that the total opportunity for these long-read applications is approximately $660 million in 2017, and growing to about $2.5 billion in 2022, a CAGR of about 30%.
  - Second, the power of improved structural variant and CNV analysis enables improved studies – and potentially accelerates discovery – in areas like rare and undiagnosed diseases, oncology, and clinical microbiology that often involve phased genomes without access to a reference.
  - Third, Illumina is committed to bringing the best sequencing solutions to market, and we believe the combination will allow both companies' technology roadmaps to accelerate as we make the most of our combined expertise, infrastructure and discoveries to shorten time to market for innovations that address critical customer needs, continue cost reduction, and integrate workflows; and
  - Finally, and importantly, both companies share an unwavering commitment to innovation and to the creation of highly accurate products. "

Key risks

REGULATORY RISKS AND TIMING

- It appears that the key risk is antitrust approval (US, potentially EU, China unlikely) and therefore the potentially lengthy deal timeline.
- Both companies provide gene sequencing solutions. However, PACB serves the long-read while ILMN serves the short-read market.
- Illumina is the biggest manufacturer of gene sequencing machines and consumables used in gene sequencing. Its machines have been used to perform 90% of all sequencing done to date.
- PacBio is a niche player in the long-read space.
- Illumina estimates that the total addressable market for long-read applications was $660 million last year, and that it could grow at a 30% compound annual rate to $2.5 billion in 2022. PACB's 2017 revenue was $93.5m with a 14% market share in the long read market.
- Other long read players with 25%-30% market share are Helicos, Oxford Nanopore and Complete Genomics (BGI of China).



- The key questions are:
  - is there substitutability between the two methods;
  - and the foreclose of competitors via bundling. Given that the two methods are also used combined, ILMN might foreclose competitors at customers via bundling.
- The sequencing read length depends on the instrument and chemistry used. The range of the read length of a short-read sequencing instrument is between 100 and 600 bp, while that of a long-read sequencing instrument varies between 10 to 15 kb. The choice one makes depends on the goal of your experiment; one isn't considered universally superior to the other.

Substitutability

- Based on industry related publications it appears there is no substitutability between the two methods therefore the long and short methods are likely to be considered as distinct product markets by regulators. Thus, the significant market share of ILMN and the incremental addition of PACB – which could cause problem if a single market would be defined for the two methods – is unlikely to be an issue.

  Genengnews: "Short-read sequencing is excellent for producing high-quality deep coverage of small to large genomes." However, he said, "The short read length limits its capability to resolve complex regions with repetitive or heterozygous sequences." As a result important biological sequences like genes or promoter regions are often highly fragmented using short-read sequencing. "The short read length also makes other computations like sequencing entire RNA transcripts or entire 16S rRNA gene sequences in metagenomics projects difficult or impossible."
  However, the longer sequences, while potentially useful in solving assembling and finishing problems, produced single-pass sequence reads with every eighth or ninth base incorrect."

- We also not that there are several potential new entrants like BGI, QGEN, Roche, Agilent etc.

In our view the merger call also confirms that there is no substitutability between the long and short methods.

- **<A >:** "Obviously, our team is going to work to close the deal as quickly as possible, and to get to close, there're a number of things that'll need to happen and our anticipation is **the long pole is going to be to make sure that we get all the relevant regulatory approvals around the world. And that's what we think will cause it to not close until the middle of next year**. But, we're going to be working to close it as fast as we can."

- **<Q>:** …"I was curious about maybe the regulatory hurdles, how we should think about that? Francis, Illumina is the largest player in this market and PacBio, Mike, is the larger of the remaining handful of competitors in this space. So, how should we think about that being a potential significant hurdle?..."
- **<A >:** "Sure. So, obviously, some of the work over the next few months is to work through the regulatory approval process in countries around the world. And the way we think about it is **we are the largest player and we provide – we serve the short-read market in sequencing. And the segments we serve are complementary to the segments that are served by the long-read players in the sense that we are uniquely qualified for the segments that we play in and we have a set of competitors in our short-reads segment**. And frankly, we don't really play in some of the long-read segments at all. If you look at de novo sequencing, for example, that's really well suited to the long-read players and there are set up players in that market and it's a vibrant market. And so, that's how we view it. They're very complementary. It adds value to our customers for us to look at a player in the long-read segment, but PacBio doesn't compete in the short-read segment; we don't compete in the long-read segment."

Bundling

- As per our reading of the industry practice the best result can be achieved via the combination of the two methods.
  Genengnews: "Dr. Schatz explained, "The longer read lengths have fundamentally more information than the short reads: infinite coverage with short reads simply won't be enough for resolving really complex regions, but just a few long reads in the right spot can solve them. The same is true for phasing haplotypes in the presence of heterozygosity or identifying proper transcript isoforms in the presence of alternative splicing."
  The scientists combined sequences generated by more conventional technology made by Illumina to help correct the mistakes in the single-molecule method. The result is "substantially better" than using Pacific Biosciences' technology alone, he said. "The data is basically perfect."

- In view there is substantial risk that ILMN will bundle its two products and so it will be able to foreclose competitors which would further increase its 80%+ market share.
- Consequently, we believe that antitrust authorities might conduct investigation whether the merger could create possibilities for exclusionary bundling or tying practices that could possibly foreclose competitors and decrease competition in the concerned markets.

The merger call also confirms this view:

- **<A >:** "As we look to the clinical market, **what we're hearing from our customers is that there are segments of the clinical market where long-read technologies do add value substantially.** So, if you look at in rare and undiagnosed genetic diseases, for example, being able to identify structural variants does help improve the diagnostic yield associated with rare and undiagnosed genetic diseases. Similarly, in clinical areas like tissue transplant, being able to sequence through the HLA region does have a benefit. And so, there're a **number of segments in the clinical market where we believe there is value in bringing the long-read technology** and we're excited about that. We've heard about that from our customers."

- As per our reading, there are two types of bundling: i) mixed bundling, ii) pure bundling:
  - Mixed bundling involves the sale of two products tied together as well as the sale of standalone components; mixed bundling can be incomplete if only one of the components, typically the tied good, is sold independently of the other - this is referred to as tying.
  - The second type of bundling is pure bundling, where the 2 products are tied, and neither is available separately.
- As per economic theory, bundling creates a cause for antitrust concerns as it can be used to protect (or leverage) market shares. There are two types of situations:
  - i) As per available literature, if bundles compete against separate components, the bundled seller might be in a position to coordinate pricing and to gain markets shares against its rivals.
    - In 2001, the EC was concerned that the merger between GE and Honeywell would allow the combined firm to better coordinate the pricing of airplane engines and avionics, and to give it advantage over engine-only and avionics-only producers.
  - ii) As per Matutes and Regibeau (1992), if there is bundle-against-bundle competition, customers face lowest prices (and company profits fall); consequently, customers benefit from lower prices, however, they lose the ability to mix and match their ideal mix of products.
    - In case of PACB/ILMN transaction, we may see similarity to the GE/Honeywell case: there is effectively no firm that is able to compete with bundled products; and consequently, it might result in further market share increase for ILMN.
      - Also, we believe that the already high market concentration increases potential tying concerns.
- In our view, it might be difficult to think of any remedies that would prevent companies from bundling products post-transaction.
  - However, we believe that regulators will definitely seek commitment to assure that smaller players are not left out of the competition (post-transaction).
  - We note that customers - research institutions, commercial laboratories, genome centers, clinical, government and academic institutions, genomics service providers, pharmaceutical companies and agricultural companies – bargaining power might mitigate the bundling issue.
- We an HSR second request highly likely and a 5-7 months antitrust timeline.

DOWNSIDE

- Other than regulatory approvals we believe the spread is mainly driven by the substantial downside. In a no deal situation we see PACB standalone value at ~$4.50 based on a pre-event 6.9x EV/Sales. We note that downside might be limited by the potential of another bidder in case of a deal break.

SHAREHOLDER VOTE

- Given the generous premium we believe (in lack of a counterbid) shareholder support is unlikely to be an issue.

COUNTERBID

- A counterbid is possible from Thermo Fisher, Agilent, Qiagen or Roche.
- However, one may argue that Agilent recently bought Lasergen, Roche already parted ways with Pacific Bio, and Thermo Fisher has been absorbed with Ion Torrent initiatives as next generation sequencing.
- Roche's hostile takeover attempt of Illumina in 2013 and the rumoured return in 2016 and prior ties to PACB might carry the risk of a counterbid for either or both of the two.

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