



PacBio Reveals Beta System Specs for RS; Says Commercial Release is on Track for First Half of 2011

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This article has been updated from a version posted Nov. 30 to include additional information from a company conference call and SEC filings.

Pacific Biosciences last week disclosed performance specifications for its "limited production release" beta instruments at early-access customer sites as part of its first quarterly earnings report since going public in late October.

The company also laid out a path for improving the read length, accuracy, throughput, and other features for the commercial release of the PacBio RS, scheduled for the first half of 2011.

As of last week, PacBio had shipped 11 instruments, to all members of its early-access program. Of those, 10 systems are already installed, and eight customers have accepted their instruments. The company expects some of them to present data at the Advances in Genome Biology and Technology meeting in February 2011.

The company said that the beta instruments produce sequence data with an average read length of 500 to 550 bases and a raw read accuracy of 80 to 85 percent, along with a consensus accuracy of 99.99 percent. Currently, beta customers are seeing an average read length of about 540 bases, with 5 percent of reads longer than 1,300 bases. The average single-read accuracy is 84 percent at present.

Over the time of the beta program — planned to be completed within six to nine months — the company will "incrementally increase the performance with consumable and software upgrades," said CEO Hugh Martin in a conference call to discuss the firm's third-quarter earnings.

He added that the commercial platform will continue to improve over time in the same manner. "We continue to be on target to reach the specifications for commercial launch in the first half of 2011," he said. "Notably, internally on our development systems at PacBio, we have achieved all of the customer release specifications."

The company has already begun to roll out new enzyme chemistry, new software features and "bug fixes" to some of its beta customers, he said, resulting in increased read lengths of 700 to 750 bases and better accuracy.

Martin did not spell out the commercial performance targets, but earlier this year, the company said the commercial PacBio RS instrument will generate average read lengths of 1,000 bases, with a small fraction of reads longer than 10 kilobases, and have a typical run time of 30 minutes ([IS 8/24/2010](#)). The

commercial instrument will also run chips with 75,000 wells, or zero-mode waveguides, whereas the development instrument uses chips with 45,000 wells. Chief technology officer Steve Turner added this week that the expected commercial raw read accuracy will be between 85 and 90 percent.

According to Martin, the hardware design for the commercial instrument is "substantially complete" and parts for the first instruments to be shipped next year are already on order. The final design includes changes based on feedback from early-access customers, "most related to serviceability and stability."

The company has also developed an enzyme chemistry "that will produce the commercial release specification" and is currently optimizing its performance internally. The new chemistry involves changes to the enzymes and dyes, and beta customers will receive several chemistry upgrades over time, allowing them to reach the commercial release performance before commercial instruments are shipped, Martin said.

Furthermore, PacBio has improved its software, and is targeting a software freeze for around the end of the year. Enhancements include increased system robustness, tools for installation and calibration, and better algorithms to minimize variability. Also, the base caller is currently being trained on data generated by the new enzyme.

Following the software freeze, "the final phase of completing our initial release will be verification and validation of the entire system, which we are planning to do in early 2011," Martin said.

Looking further into the future, Turner said that through a combination of chemistry advances and better algorithms, the raw read accuracy will improve "beyond" 85 to 90 percent. Using present engineering methods, the company also sees "a pathway" to get to a raw read accuracy of 95 percent. "Beyond that, we would need to switch to new methods, for example in the area of protein engineering," he said.

Turner also said that the firm is working to increase the yield of zero-mode waveguides filled with a single active polymerase enzyme beyond 30 percent by developing a "super Poisson" technology, where each well has a mounting point that can accommodate only one polymerase. He said the company already has "good proof of principle on demonstrating this mounting point" and is now combining it with the sequencing technology.

One important lesson from the beta program so far, Martin said, is that "single-molecule work requires stringent controls around sample prep." Single-molecule sample prep is "a tricky thing," and to minimize the variability that some customers experienced, the company has modified its sample prep protocols and supporting documentation, he added.

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The company has also invested "significantly" in service and support for both beta and commercial customers, Martin said, including a toll-free tech support number, an online customer portal with documentation, and a customer discussion forum. It has trained application specialists and service engineers, established a troubleshooting workflow based on lessons learned from the beta program, enabled remote diagnostics on the instrument, and hired additional field personnel. One of the early-access instruments — at the National Cancer Institute — was installed in only eight days prior to its acceptance by the customer, Martin reported.

Martin declined to provide information on the development of or timeline for RNA or methylation sequencing applications, saying that the company's policy is not to discuss unreleased products.

Commenting on PacBio's competitive position compared to other sequencing platforms, Martin said that the firm is initially targeting customers who want long read length, fast results, and the ability to do many experiments at a low cost per run. "Initially, because we are not going to be in the same throughput war that some of the second-gen platforms are in, we are focusing on our differentiators," he said.

Compared to Sanger sequencing, he said that PacBio will "meet or beat" Sanger's read length and cycle time, and have a "much higher" throughput and "much lower" cost per base. He did not compare the two technologies' accuracies.

Regarding applications of the PacBio platform, Martin said that the three most important ones to date are infectious disease research, cancer research, and SNP validation.

Infectious disease researchers have been moving from genotyping to sequencing "as a way to get a much more definite result," he said, and "a big driver" for PacBio in this area is the fast turnaround time of its instrument, compared to second-gen sequencing platforms. In cancer research, he said, long reads are "extremely important" to be able to distinguish between subpopulations in the same tumor. And researchers are expected to use the PacBio technology to validate SNPs from sequencing human genomes by short-read technologies because it provides an orthogonal method with different systematic errors.

In preparation for its commercial launch, the company has also increased its sales force from six in the second quarter to 11 in the third, who are currently spending about half their time "managing the customers that are in our backlog," Martin said. The company also has to "manage the demand" from potential customers in parts of the world it currently does not serve. "Despite how badly someone in, say, Japan right now might want to buy even multiple systems, we want to be thoughtful about that," he said.

Losses Widen in Q3

For the quarter ended Sept. 30, PacBio reported a net loss of \$40.7 million, a 66 percent increase over a \$24.5 million loss for the same period last year that resulted from an increase in materials costs and an expansion of its sales, services, and manufacturing operations in advance of the commercial launch of the PacBio RS.

Revenue for the third quarter was \$220,000 — due solely to research grants — compared to no revenue for the same period last year. The company has not yet received revenue from product sales, and reiterated that it does not expect to do so before the end of the year.

Chief financial officer Susan Barnes explained during the call that under the terms of the beta program, the company is entitled to 50 percent of the selling price of the RS instrument — all are sold at the \$695,000 list price — upon customer acceptance of the beta unit, and will recognize the full sales price when the instrument is upgraded to commercial release specifications, which is expected to happen during the first half of 2011.

As of Sept. 30, 2010, the company's backlog of purchase orders or signed contracts was approximately \$20 million, or 32 instruments — an increase of \$5 million since June 30 ([IS 9/28/2010](#)). This backlog excludes 10 percent of the purchase price, which the company plans to recognize as service revenue during the 12 months following the installation and acceptance of the systems.

In documents filed with the US Securities and Exchange Commission this week, PacBio said it expects to deliver all orders in its backlog by Dec. 31, 2011.

Customers who have placed orders for commercial instruments include genome centers, academic centers, agricultural companies, and service providers. Several companies have disclosed their purchase orders, such as Monsanto, which is also a PacBio investor, as well as service providers Expression Analysis and GATC Biotech.

PacBio's research and development expenses in the third quarter increased 56 percent, to \$32.9 million from \$21.1 million during the year-ago period, due to increased personnel in manufacturing and operations, increased costs for prototype components and instrument and consumables products, and facilities and information technology.

Selling, general, and administrative expenses more than doubled to \$8 million, from \$3.4 million for the same period of 2009, primarily due to growth in sales and customer support personnel, travel and promotion, and facilities and information technology.

The company said that it hired 146 employees over the past year, bringing its total workforce to 406 staffers as of the end of the third quarter.

As of Sept. 30, PacBio had \$112.9 million in cash and investments, however, this does not include the approximately \$210 million it raised in its IPO at the end of October ([IS 11/2/2010](#)). Following the offering, the company's underwriters exercised their over-allotment options, purchasing another 1.875 million shares at \$16 per share.

The company currently does not provide a financial forecast but plans to do so once it begins selling products and can better estimate future revenues and margins.

In this week's SEC filing, PacBio also commented briefly on its litigation with Affymetrix, which filed a suit against the company last month for unlawful recruiting of its employees ([IS 11/9/2010](#)). "We believe the Affymetrix complaint is entirely without merit and intend to vigorously defend ourselves against Affymetrix' claims," PacBio said, noting that as of Nov. 29, it had not been served with a copy of the complaint.

— *Monica Heger contributed to this article.*

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