



Pacific Biosciences HiFi Reads Drive Core Lab Business, High-Flying Stock Price

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This story has been updated to include news of a large instrument purchase by the UK's Wellcome Sanger Institute and a commitment to whole-genome sequencing with PacBio's HiFi reads.

NEW YORK – Over the last year, core genomics labs have seen massive interest in sequencing on Pacific Biosciences' Sequel II platform, driven by HiFi reads, a new data type launched in late 2019.

HiFi reads, a distillation of high quality PacBio long reads that can reach 99.9 percent accuracy, are taking over that segment of the market for many service providers.

"I have had one request all year for continuous long reads," said Molly Zeller, a research specialist at the University of Wisconsin-Madison's Biotechnology Center DNA Sequencing Facility. "Everything else has been for HiFi. It's HiFi or bust." The lab's PacBio data output in 2020 increased about twelvefold, she estimated.

While shorter than the longest possible reads obtainable on PacBio's platform, generating HiFi reads does not require as much expertise in extracting high molecular weight DNA, making them accessible to a wider set of researchers, said Dave Kudrna, associate director and project manager at the University of Arizona's Arizona Genomics Institute.

Their popularity is driving business, to the point that wait times are increasing. "We have queries every week, 10 to 20 people a week emailing us," Kudrna said. "Our queue is out into July right now. We should probably buy another machine."

Interest in HiFi reads has led to new instrument purchases. Since the end of 2019, the majority of inquiries have been for HiFi reads, Edinburgh Genomics Service Manager Javier Santoyo-Lopez said, but with a Sequel I, the lab couldn't deliver them. The university made a strategic play to obtain a Sequel II and several primary investigators applied for a grant to help acquire a Sequel IIe, a new instrument that generates HiFi reads directly.

Edinburgh Genomics was one of three UK-based core labs that announced Sequel II instrument purchases in December, joined by the University of Liverpool Centre for Genomic Research and the Oxford Genomics Centre.

And this week, the UK's Wellcome Sanger Institute announced it would purchase seven Sequel IIe instruments and upgrade five existing Sequel II instruments so researchers could generate more HiFi reads to support several sequencing projects, including the [Darwin Tree of Life](#) and the aquatic symbiosis genomics programs.

"Our investment in the Sequel IIe represents a massive scale-up in our long-read sequencing capacity," Cordelia Langford, director of scientific operations at the Sanger Institute, said in a statement. "The instruments allow us to advance our operational capacities to deliver to projects across the Sanger portfolio, including human and pathogen genomics as well as, especially, Tree of Life."

HiFi reads' growing popularity has also coincided with rising fortunes for PacBio. A year ago, a \$1.2 billion acquisition bid from Illumina [fell apart](#) due to resistance from US and UK regulators and a new management team was brought in over 2020 to pick up the pieces. On the Nasdaq, shares of PacBio have risen nearly 600 percent over the last 12 months to \$33.91.

The company's success in 2020 is "directly attributable to HiFi reads," said Luke Hickey, PacBio senior director of strategic market. "Just from a market adoption perspective, HiFi is becoming the preferred sequencing data type for whole-genome sequencing. That's creating demand for the Sequel IIe in core labs as well as production-scale genome centers. That enthusiasm has translated into purchases and purchases have translated into broader excitement outside the research community."

Introduced with the Sequel II platform in early 2019, the HiFi protocol selects the subset of circular consensus sequencing (CCS) reads with quality above Q20. The firm described its [CCS protocol](#) in a *BioRxiv* preprint in January 2019 and published a paper on HiFi reads in *Nature* in August 2019.

HiFi reads are accurate enough to detect single nucleotide variants while also offering the read lengths long enough to detect structural variants. On the Sequel II instrument, these are generated in computing clusters, but on the [new Sequel IIe instrument](#), launched in October 2020, they're generated on the machine.

HiFi reads "are better than Sanger" sequencing, Kudrna said. "Nothing on the planet can beat it. If you're really interested in what a whole genome looks like, this is the way to go."

"They're still more expensive than Illumina [sequencing], but have leveled the accuracy part of the equation," he added.

At UW-Madison, a PacBio certified service provider, HiFi reads are driving business. "Revenue from PacBio has definitely increased" in 2020, Zeller said. The core lab's prices increased 61 percent year over year, she said, but customers are getting much more data. The price per gigabase fell from approximately \$81 to \$7, she said.

Arizona Genomics Institute hasn't seen business increase because their instrument is almost always running at full capacity, but interest grew over the last year, Kudrna said. Though AGI is a certified service provider — especially for the agricultural genomics community — and a research and development partner for PacBio, it is primarily a research lab, which has factored into the decision not to buy another machine at this time, he said.

Zeller said her lab is "discussing options" for acquiring another instrument. "I've been pushing my boss really hard," she said.

With its Sequel IIe installed now, Santoyo-Lopez said that Edinburgh Genomics expects to see a "nice increase" in projects in 2021. "We have quite a few people coming to us to ask

about HiFi projects," said Santoyo-Lopez. "It's not all the time the phone is ringing, but it's quite a lot."

With more efficient reagents and HiFi reads generated directly off the instrument, "there's going to be savings from the point of view of the user," Santoyo-Lopez said. And the lower costs could help the lab, too. "Because the data footprint is smaller, it's probably going to bring in more business," he said.