

# DNA Sequencing Technologies

COMPANIES: A, ILMN, LIFE, RHHBY, ROG VX, PACB



ILMN'S  
DNA SE-  
QUENCING  
BUSINESS;  
LIFE

## ILMN Purchases Outpace Competitors

**Purchases of Illumina's HiSeq 2000 are expected to remain strong through the 1H11 because of the machine's high throughput, despite some initial growing pains, and NGS/SMS consumable and reagent budgets are continuing to ramp in 2011.**

- OTR Global's reads on ILMN's DNA sequencing business and LIFE are positive, as in the September report
- ILMN dominates NGS purchases, with 9 institutions already having HiSeq 2000s and 8 institutions planning at least 9 HiSeq 2000 purchases by end of 1H11 (including 6 in 1Q11)
- LIFE's 5500 gaining interest among 4 SOLiD users, with all planning to upgrade by 2Q11
- 4Q10 budgets for consumable and reagents up 24%–27% qq, with 1Q11 budgets expected up 28%–31% qq
- Areas to Watch: ILMN's MiSeq and pre-owned GA2Xs may impact adoption of LIFE's Ion Torrent Personal Genome machine because of potential for improved read length, throughput and cost effectiveness

### EXECUTIVE SUMMARY

Despite some initial set-up and run issues, demand for **Illumina Inc.**'s HiSeq 2000 is expected to remain strong through 1H11, with six purchases planned in 1Q11, one planned in 2Q11 and two planned sometime in 1H11. In addition, nine institutions already have purchased the machine. Upgraded HiSeq 2000 chemistry and lower cost sample preparation kits are expected to drive further adoption of the machine. In addition, launch of the company's MiSeq and resale of used GA2Xs may affect the adoption of **Life Technologies Inc.**'s Ion Torrent Personal Genome machine because of lack of information on the Personal Genome machine's sample preparation, throughput, and error rate. However, three sources anticipate purchasing the Personal Genome machine in 1Q11, and Life Technologies' 5500 upgrade is garnering interest among all four SOLiD 4.0 users, with upgrades anticipated during 2Q11.

### KEY DATA

#### ILMN HiSeq 2000 Demand Remains Strong

Purchases	1Q11	2Q11	1H11	2H11	2012	DON'T KNOW	TOTAL
ILMN's HiSeq 2000	6	1	2	-	-	-	9
PacBio's SMRT Technology	-	1	-	1	1	2	5
LIFE's 5500 upgrade	-	4	-	-	-	-	4
LIFE's Ion Torrent's Personal Genome machine	3	-	-	-	-	-	3
Brand undecided	-	-	-	1	-	-	1
None	-	-	-	-	-	-	2

### SOURCES & BACKGROUND

**18 institutions**, comprising 12 academic genome centers (3 large, 3 midsized and 6 small) and 6 academic core facilities (3 midsized and 3 small)

**REPEAT SOURCES** 13 (5 from OTR Global's January note and 8 from September report)

**INTERVIEWS** Early to mid-January

**AVERAGES** Straight

"We also have a large number of HiSeq 2000s, which are replacing our GA2Xs. We have one up and running daily, with the other ones delivered in December taking a little longer to get up and running."

*Director at large academic genome center*

See last page for Important Disclosures and Analyst Certification

# DNA Sequencing Technologies

## HiSeq 2000 Purchases Remain Strong

As in September, Illumina continues to dominate the NGS purchases, with 15 institutions using the GA2X and nine using the HiSeq 2000, as well as eight institutions planning at least nine HiSeq 2000 purchases (six purchases in 1Q11, one in 2Q11 and two sometime in 1H11). In addition, smaller genome centers and core facilities continue to adopt the HiSeq 2000, despite the high price tag, as high throughput remains the key driver of purchases. "We got our HiSeq 2000, and we have it up and running now. There were a couple snags with the flow cells, but the last run we just did was pretty good. We are doing a paired end run tomorrow," said a mid-sized academic genome center's director.

Nearly all sources with HiSeq 2000 in place noted problems with the set-up and initial runs. Some were attributed to issues with non-uniform cluster densities on the flow cells, but others noted other hardware and sample issues. However, the company has resolved the flow cell issue at most institutions and is helping all laboratories with any other problems with initial set-up and runs. In addition, no source said these initial problems would prevent additional purchases of the HiSeq 2000 or other Illumina products. "We also have a large number of HiSeq 2000s, which are replacing our GA2Xs. We have one up and running daily, with the other ones delivered in December taking a little longer to get up and running. We know these machines work; it is just a matter of getting them to the level of the first one. This is not hindering us from getting any more HiSeq 2000s because the cost benefit is just so much greater than the GA2X. The economics of the HiSeq2000 are just too good. We are really aiming to get as many as possible," one director said. Another said, "We are not discouraged with the company, as we believe this will be the platform of choice for the next couple of years because the output is so attractive. It is just a matter of getting it to run properly."

Six institutions planning HiSeq 2000 purchases are expected to trade in their GA2X for the device, but trade-in value remains unclear. "We are planning on trading in another GA2X for a HiSeq 2000 and then going to buy another HiSeq 2000 in the next three to four months," one director said. Another said, "We might trade in the other GA for another HiSeq in about nine months because we expect the throughput to be so much greater with the HiSeq 2000."

## SOLiD Users Upgrading to 5500 in 1H11

Four institutions are using Life Technologies' SOLiD 4.0, and all expect to upgrade to the company's higher-throughput 5500 model in 2Q11. "We will be upgrading our SOLiD 4.0s to 5500s this year, probably in the first half of the year. The specs on the machine are pretty well known," said a mid-sized academic genome center's director. Another said, "We'll probably upgrade to the HQ 5500 later this year."

Several sources remain interested in Life Technologies' Qdot technology but are still unclear about the launch date and when initial data will become available. The new single molecule sequencer (SMS) might pose a threat to **Pacific Biosciences of California Inc.**'s SMRT technology and **Roche Holding Ltd.**'s 454 because of the device's continuous tunable reads; however, most researchers are waiting for a scalable device and run data.

Sources remain concerned with the lack of information on Ion Torrent's Personal Genome machine's sample preparation, throughput and error rate. "I am currently looking into purchasing an Ion Torrent machine but remain undecided because the company has not been upfront regarding the sample preparation and other specs. I am still considering it, though. I just need more informa-

### INITIAL PROBLEMS HAVE MINIMAL IMPACT

"We got our HiSeq 2000, and we have it up and running now. There were a couple snags with the flow cells, but the last run we just did was pretty good. We are doing a paired end run tomorrow."

*Mid-sized academic genome center's director.*

# DNA Sequencing Technologies

tion,” said one researcher at small academic genome center. However, three institutions plan on purchasing the machine in 1Q11.

Illumina recently launched its MiSeq, which is another low-cost approach with a capital investment cost of \$125,000 that can generate up to 1.5 GB of data per run at a cost of about \$500 for consumables and reagents. Although a couple sources said this would compete with Life Technologies’ Ion Torrent Personal Genome machine among smaller institutions, the MiSeq may also serve as a test run machine at large institutions. “Illumina recently launched their MiSeq technology, which will probably be popular among a subset of laboratories. I think it will be applicable for smaller-sized laboratories as well larger-sized laboratories who ... may use it to test run the sample before doing full run on HiSeq 2000. It will only take one day to run, and the researcher can quantify the library and use the results to set up the run on the HiSeq 2000,” one director said.

Illumina also is selling traded-in GA2xs at a much lower cost, approximately \$125,000 according to one researcher, which may also compete with the Personal Genome machine. “Regarding Ion Torrent, it’s not a good buy. A GA2X would be cheaper per run for a smaller lab,” said small academic genome center’s director. A midsized academic genome center’s director said, “I have heard that Illumina is reselling traded-in GA2Xs for a much lower price, which makes sequencing much more affordable for a smaller lab. I would much prefer to buy a GA2X than to buy an Ion Torrent machine.”

## NGS Purchases Ramp Despite Funding Concerns

Overall NGS purchases remain strong, with 13 institutions planning machine purchases during 1H11. Nearly all repeat sources from the September report said purchase plans were in line with their previous expectations. Three institutions are using Roche’s GS FLX (454) with or without the titanium upgrade, with no institutions planning a GS FLX purchase in 2011.

In terms of NIH/NSF stimulus funding or grant funding, most sources were unclear of the funding environment for 2011 compared with 2010, but four sources said the environment would be the same, while one thought it would be slightly better and two said it would be slightly or moderately worse. “I am not sure of the funding environment. It still remains a challenging situation, but we didn’t have a bad year last year. I don’t think it is going down or up, probably, remain about the same. We also get a lot of private funding, large donations,” said a large academic genome center’s director. Another director said, “The funding environment is concerning. We are concerned with the new Republican House [of Representatives], that the big bolus of money that went out last year will not be available this year and we will go back to funding levels before the stimulus was available, if not below those levels.”

However, nearly all sources have been able to find funding for NGS and SMS purchases, despite changes in government funding. “We have always been able to find money if we really wanted to buy something. If you look how we bought the HiSeq 2000, we applied for a grant, got a good rating but didn’t know if we would get it or not, so we went out and got some money together and bought it first before we knew about the grant. If we get the grant, we will pay ourselves back,” one director said.

## Strong NGS Consumable/Reagent Growth Continues

Consistent with OTR Global’s previous findings, nearly all sources expect 2011 NGS consumable and reagent budgets to grow, with the nine sources who provided numerical data expecting a 55%–58% increase yy. “Our budget for NGS consumables and reagents continue to increase year

### ILMN’S MISEQ

“Illumina recently launched their MiSeq technology ... I think it will be applicable for smaller-sized laboratories as well larger-sized laboratories who ... may use it to test run the sample before doing full run on HiSeq 2000. It will only take one day to run, and the researcher can quantify the library and use the results to set up the run on the HiSeq 2000.”

*Director*

# DNA Sequencing Technologies

to year and will continue to do so as we expand our capabilities and improve upon our technologies,” said a large academic genome center’s director. A midsized center’s director said, “We have added a number of machines, so I anticipate that our consumable and reagent budgets will be up greatly.”

Overall, institutions said 4Q10 budgets for consumable and reagents increased an average 24%–27% qq, with 1Q11 budgets expected to be up an average 28%–31% qq, in line with September predictions. (Sources were much better at projecting quarterly budgets for consumable and reagents as opposed to full-year estimates due to potential purchases and types of studies being completed.)

Exome and whole genome sequencing continue to dominate NGS use, with other advances and multiplexing ability driving use of genotyping on NGSs. “Whole genome and exome sequencing is really the trend right now, and I don’t see that slowing down anytime in the near term,” a researcher said. Another said, “Exome capture is really huge right now. In addition, researchers are starting to use NGSs for genotyping because of multiplexing capabilities. It is possible that these capabilities will really drive microarrays out of the picture. No grants after 2012 will include microarrays, and I don’t expect anyone using microarrays after 2014. Currently, the cost of microarrays is becoming more comparable with NGS technologies, and the throughput and accuracy is so much greater with NGS that it is not cost effective to use microarrays anymore.”

In addition, agriculture studies using NGS technologies appear to be gaining. “We’ve never had a lot of medical research on our campus; it’s mostly agriculture, and they are using NGS more now,” said a midsized academic genome center’s director.

Illumina recently announced the launch of new chemistry that will improve HiSeq 2000 throughput. “Illumina just launched new chemistry five days ago that will give us one TB of sequence per run,” one director said. Another said, “Illumina is also tweaking their chemistry a bit to get 1 TB reads, which I believe will be a combination of two full runs on two flow cells, so 500 MB reads on each flow cell.”

In addition, Illumina has also been offering lower pricing for sample preparation kits. “Illumina recently lowered the pricing on their sample prep kits, including their mRNA and small RNA sequencing kits,” one director said. Another said, “I was using **New England BioLabs [Inc.]** for some of our consumables and reagents, but now with the launch of Illumina’s TruSeq sample prep kits, that is going to be harder because they will not be selling the adapters separately as they previously did. For now, we will use our old approach and buy the adapters separately, but we ultimately are going to move over to using the TruSeq because the company aggressively cut the cost per sample price.”

Two sources performing exome sequencing have started using Illumina’s new exome sequencing kit, which some anticipate to hurt use of **Agilent Technologies Inc.**’s and Roche/Nimblegen’s sequence capture technologies. “For exome sequencing, I’ve already ordered the new kit from Illumina. I was using Agilent for targeted sequencing, but I’m going to try the exome sequencing kit from Illumina. I haven’t received it yet,” a researcher said.

## PacBio Little Impact on Illumina or Life

Pacific Biosciences continues to pose a minor to moderate threat to NGS technologies, with a greater impact expected later in 2011 and early 2012. However, sources said Illumina’s GA2X and HiSeq 2000 as well as Life Technologies’ SOLiD will maintain a significant presence in the gene expression market, while Roche’s 454 will be harder hit, with many institutions waiting to

“No grants after 2012 will include microarrays, and I don’t expect anyone using microarrays after 2014. ... It is not cost effective to use microarrays anymore.”

*Researcher*

## KEY GROWTH DRIVERS

# DNA Sequencing Technologies

see adoption and troubleshooting among Pacific Biosciences' beta sites. "The impact of Pacific Biosciences will be on longer read technologies such as Roche's 454 as well as other upcoming single-molecule sequencing technologies. It is not likely to have an impact on the shorter-read technologies such as GA2X, HiSeq 2000 and SOLiD 4.0," one director said.

---

This report was researched and written by **Beth Gilbert**, with additional reporting by **Julie Remington** for OTR Global LLC.

OTR



# DNA Sequencing Technologies

## ON NGS USE/ADVANCES

“There continues to be a growing base of NGSs because smaller to midsized institutions are adopting these technologies, so new entries are really increasing the install base, especially with the junior models such as Roche’s GS FLX Junior, Illumina’s MiSeq, and Life’s Ion Torrent. These machines are making it more affordable for researchers with less funding to purchase these machines.” *Researcher at a large academic genome center*

## ON NGS/SMS PURCHASE PLANS

“I think over the next few months, we may get one or two more HiSeq2000s, but we expect to have a larger number over the next year.” *Director at a large academic genome center*

“We’ll trade in a GA for another HiSeq. The GAs are going for about \$150,000 now, and they are selling. I think smaller labs are buying them.” *Director at a midsized academic genome center*

“We just applied for a grant to get a PacBio on our campus. We are currently getting one on another campus, but we want to get one on our campus, probably in another year from now.” *Director at a midsized academic genome center*

## ON INITIAL HISEQ 2000 USE

“Our HiSeq 2000 was delivered, and ... we are trying to get it to run. It has been problematic outside the test run. The test run went well but only had two decent runs, as our three other runs were problematic. So the track record so far has been not that good. Yet, the good runs gave us great results, so we are confident we will get there, but we just don’t know if it is hardware problem or our samples.” *Director at a midsized academic genome center*

“We are not running the HiSeq2000s we currently have daily, they are all running at some point or another but having issues. We are going to continue going ahead with the conversion; we’re not changing our mind on our decision to convert our machines, it is just frustrating. The cost model associated with the HiSeq is too good. We will sort this out.” *Director at a large academic genome center*

## ON LIFE TECHNOLOGIES’ ACQUISITION OF ION TORRENT AND QDOT TECHNOLOGY

“It is really early to say, but it will depend on the data they come out with. It could compete with Pacific Biosciences’ SMRT technology as well as Roche’s 454, but that remains to be seen. I am a little concerned with the effect of the quantum dot on the DNA polymerase.” *Director at a midsized academic genome center*

“The cost of Ion Torrent’s machine is \$50,000, but there is an added cost for peripherals that run approximately \$15,000, so the total cost of the machine is approximately \$65,000. However, the throughput is not going to be there for awhile. It is something in the range of 100–500 MB per run, so it would be better to buy a used GA2X at this time if you were considering an Ion Torrent.” *Director at a midsized academic core facility*

## ON CONSUMABLE AND REAGENT BUDGETS

“Although Illumina dropped the prices on their kits dramatically, we’ll have much greater throughput and we’ll be doing a lot of multiplexing, so we may see at least a 5% increase in the first quarter.” *Director at a midsized academic core facility*

## ON PACIFIC BIOSCIENCES’ BETA-SITE AND COMMERCIAL LAUNCH IMPACT

“The technology still needs some work, which may delay the impact on longer-read sequencing technologies.” *Director at a midsized academic genome center*

# DNA Sequencing Technologies

## 1. Which next-generation DNA sequencer (NGS) are you using for your DNA sequencing needs? (Some sources gave more than one answer.)

ILMN's GA2X:	15
ILMN's HiSeq 2000:	7
LIFE's SOLiD 4.0:	4
Roche GS FLX (454):	3
PacBio's SMRT technology:	2
Outsourcing, Roche 454:	1
Outsourcing, SOLiD:	1

## 2. Do you expect your 4Q10 and 1Q11 budgets for NGS/SMS genomic consumables and reagents to increase, decrease or remain the same qq?

	4Q10	1Q11
Up 91%–100%:	1	1
Up 41%–50%:	-	1
Up 31%–40%:	1	-
Up 26%–30%:	-	1
Up 21%–25%:	1	3
Up 16%–20%:	3	1
Up 11%–15%:	1	-
Up 1%–10%:	1	1
Up 1%–5%:	1	1
Up:	6	7
Flat:	1	1
Not applicable:	2	1
<b>Average:</b>	<b>Up 24%–27%</b>	<b>Up 28%–31%</b>

## 3. Do you expect your 2010 budget for NGS/SMS genomic consumables/reagents to increase, decrease or remain the same yy?

Up 91%–100%:	2
Up 71%–80%:	1
Up 51%–60%:	2
Up 41%–50%:	1
Up 31%–40%:	1
Up 21%–25%:	1
Up 6%–10%:	1
Up:	8
Not applicable:	1
<b>Average:</b>	<b>Up 55%–58%</b>

## 4. LIFE Technologies anticipates the launch of their new 5500 by 1Q/2Q11. Do you plan on upgrading to the HQ upon availability?

No plans to upgrade/purchase:	14
Upgrade 1Q11:	1
Upgrade 2Q11:	3

## 5. How will LIFE technologies SMS nucleic acid sequencing by synthesis approach using Quantum-dot (Qdot) technology compete with other sequencing technologies such as Pacific Biosciences SMRT technology? (Some sources gave more than one answer.)

Potential threat to Roche's 454:	9
Potential threat to Pacific Bioscience's SMRT technology:	8
Not a potential threat to NGS/SMSs:	3
Don't know:	6

## 6. Has Pacific Biosciences missed the opportunity to be competitive due to upgrades on short read sequencers and new longer read sequencing technologies or will they pose a threat to the marketplace?

Pose a threat to longer read sequencing technologies:	12
Don't know:	6

# DNA Sequencing Technologies

## ANALYST CERTIFICATION

The Author(s) of this research report certify that all of the views expressed in the report accurately reflect their personal views about any and all of the subject securities and that no part of the Author(s) compensation was, is or will be, directly or indirectly, related to the specific recommendations or views in this report.

## ADDITIONAL DISCLOSURES

OTR Global LLC is an investment advisor subsidiary of OTR Global Holdings II Inc. OTA Financial Group LP is the controlling shareholder of OTR Global Holdings II Inc. OTA LLC is a registered broker dealer subsidiary of OTA Financial Group LP. The affiliated companies of the OTA Financial Group LP, OTR Global Holdings II Inc. and/or its principals, employees, clients or researchers may have an interest in the securities of issuers discussed herein or in securities of other issuers in other industries. The affiliated companies may provide bids and offers for securities of the subject company(ies) discussed in this report and may act as principal in connection with such transactions. The affiliated companies, its principals and/or employees may also hold a position (long or short) in the shares of the subject company(ies) discussed in this report.

OTR does not financially compensate sources for participating in its research reports. OTR conducts industry events where sources who participated in OTR's research reports may be compensated or have their expenses paid by OTR to attend the industry event. Additionally, sources who participate in OTR's research reports may directly interact with clients at these OTR industry events.

**©2011 OTR Global LLC (OTR).** All rights reserved. This report was produced for the exclusive use of OTR and may not be reproduced, electronically or via hard copy or relied upon, in whole or in part, without written consent. The information herein is not intended to be a complete analysis of every material fact in respect to any company, industry or the subject discussed, nor by itself sufficient upon which to base an investment decision. OTR uses a set of symbols to represent its read: Thumb Up denotes positive, Thumb Down denotes negative, and Fist denotes mixed. These symbols are not a recommendation to buy, sell or hold a security.

Additional information available upon request.