CRACKING THE CODE

The cost and speed of DNA sequencing is nearing a point where it is rapidly becoming economical for clinical trials and cancer management. It's also expected to move into primary care physicians' offices, a sweet spot for big pharma. **Marc Iskowitz** on some of the hurdles that must be overcome for these instruments to play a wider role

Paul Billings has a message for big pharma: speed can cure. Rapid genetic analysis of the type delivered by DNA-sequencing firms like Billings' company, Life Technologies, "will bring information to the fore that will really help patients…in real time in ways that haven't been possible," the chief medical officer asserts.

For the pharma industry, burdened by a discovery process that takes more than a decade and a couple of billion dollars to produce a new cure, Billing's advice could hit home.

His is one of a few dozen firms expediting development of the sub-$1,000 genome—sequencing the chemical base pairs of every letter of DNA in a person's genome at a price and speed experts say could make this diagnostic tool more accessible, and possibly hasten the day when MDs will be able to utilize it in medicine.

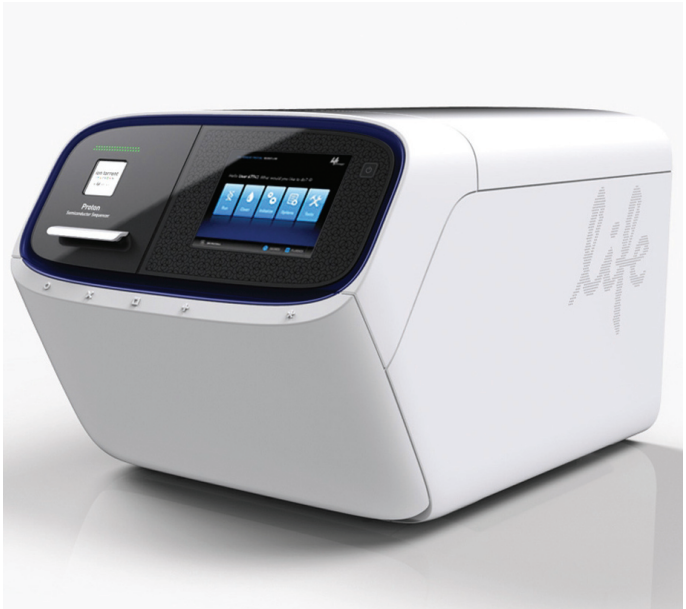
Sequencing is being used by big reference labs and by drugmakers to design genetic-specific

treatments with companion diagnostics and to hone clinical trials to patients most likely to respond to therapy. But our industry is still trying to figure out the right way to transition sequencing from lab to clinic.

That's one reason Roche attempted a hostile takeover of San Diego-based Illumina in January of this year. Illumina CEO Jay Flatley rallied stockholders to reject the takeover in April, much to the chagrin of Roche chairman Franz Humer.

"Roche continues to be fully committed to the life sciences field," the Swiss firm said in a statement. "We also continue to believe in the future potential of sequencing in the clinical setting. Roche has been investing and will invest in its existing technologies."

It's unlikely that Humer will make another play for Illumina. Most pharma companies, rather than commit to one specific platform at this stage, want to ensure their drug and companion diagnostic work on any sequencing platform.



"If you're a big pharma, you don't want to be a sequencing player," says Jerry Isaacson, a senior healthcare analyst with research outfit GlobalData.

Still, the hostile bid may have been a sign of things to come. "We're going to see more of these Roche-like attempts, and other partnerships that would enable pharma companies to go to market with a test that's alongside the actual product," predicts Nancy Steele, Pfizer VP of strategy.

Molecular diagnostics is starting to drive drug sales. Witness the approval of Pfizer's Xalkori (crizotinib) last year for treatment of some patients with late-non-small cell lung cancer with a genetic mutation that can spur the growth of cancerous cells. The agency simultaneously approved a test from Abbott Molecular Diagnostics for the mutated gene, called ALK (anaplastic lymphoma kinase).

Pfizer's reps aren't the only ones carrying these products in their bags. Genentech's melanoma drug Zelboraf (vemurafenib) was also approved in 2011 with a test from Roche Diagnostics to screen for the BRAF V600 mutation. Further back in the pipeline, GlaxoSmithKline is working with Life Technologies to develop a companion diagnostic for use with cancer drug GSK1572932A.

As sequencing gets cheaper and scientists can read the results faster, doctors one day may be able to prescribe combination therapies geared toward multiple mutations to head off other diseases, as opposed to drugs like Zelboraf and Xalkori focused on single aberrations linked to cancer.

"Lower costs, better ease of use and faster runs will open new markets," said Illumina in a letter to shareholders.

When the Human Genome Project produced a finished sequence of the genome back in 2003, a massive 13-year undertaking, the project cost a colossal $3.8 billion (that's $10 billion in 2010 dollars, according to one estimate).

My, how things have changed. Life Technologies has pledged to release a benchtop machine later this year, the Ion PGM (Personal Genome Machine), which it says will be capable of mapping a genome for $1,000 in a matter of hours. It's planning on getting it ready for submission to regulatory agencies later this year, with potential approval in 2013.

The PGM melds speed, accuracy and a lower price point (it's $50,000 and is the size of a large desktop printer; most machines cost hundreds of thousands of dollars and are at least the size of small refrigerators).

Another firm, British outfit Oxford Nanopore, said that within the year it would release a disposable gene sequencing device that is the size of a USB memory stick and plugs into a laptop computer. Expected cost: under $900.

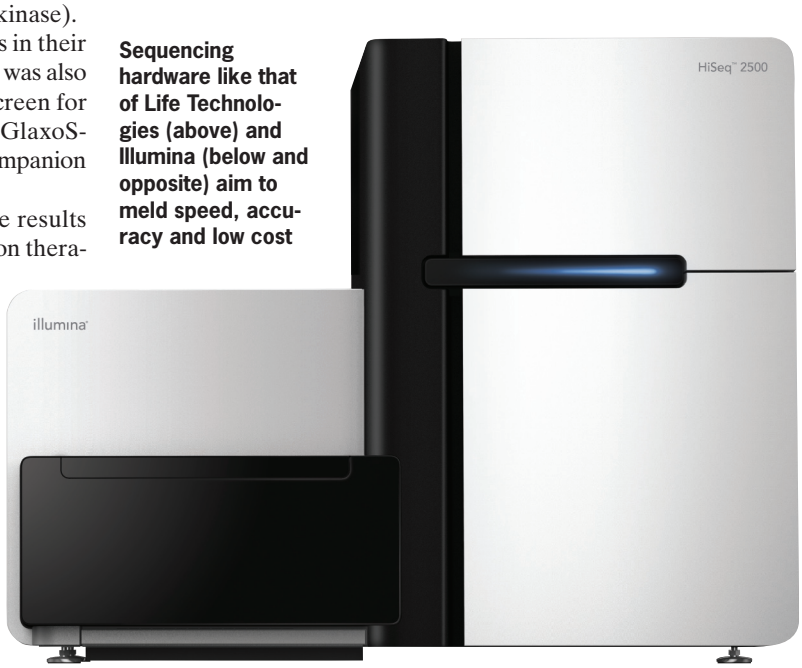
"Regardless of which technology makes it to the lead…the fact that sequencing is getting much faster and more accessible is a significant advance in terms of taking what we know about the genome and using it to make drugs and tests that are tailored for patients," says Vamil Divan, a VP and senior analyst at Credit Suisse.

Hurdles remain for these instruments to play a wider role. High-throughput computing power, such as that offered by cloud computing, is becoming available to do the number-crunching. But the last step—review by a genetic counselor or physician to sort through the sequence and make decisions about what is actionable—will always be the longest.

In addition, MDs have yet to get educated about how sequencing information is used, and sequencing will move into the large reference labs like Quest and LabCorp, as well as major medical centers and large hospitals, long before it arrives in doctors' offices. What's more, no sequencers have been cleared by FDA.

All of this means that, "For diabetes, common-variety heart disease and other things like that, we still have another five years to go before we see broad-based adoption in clinical settings," explains Billings.

Until then, we're left pondering the possibilities: "Imagine if you're a doctor and you can say to a patient, 'Depending on your genetic sequence, you can get any of these drugs which are guaranteed to work,'" says Isaacson. "It's not science fiction any more. It's a matter of time." ■



Sequencing hardware like that of Life Technologies (above) and Illumina (below and opposite) aim to meld speed, accuracy and low cost