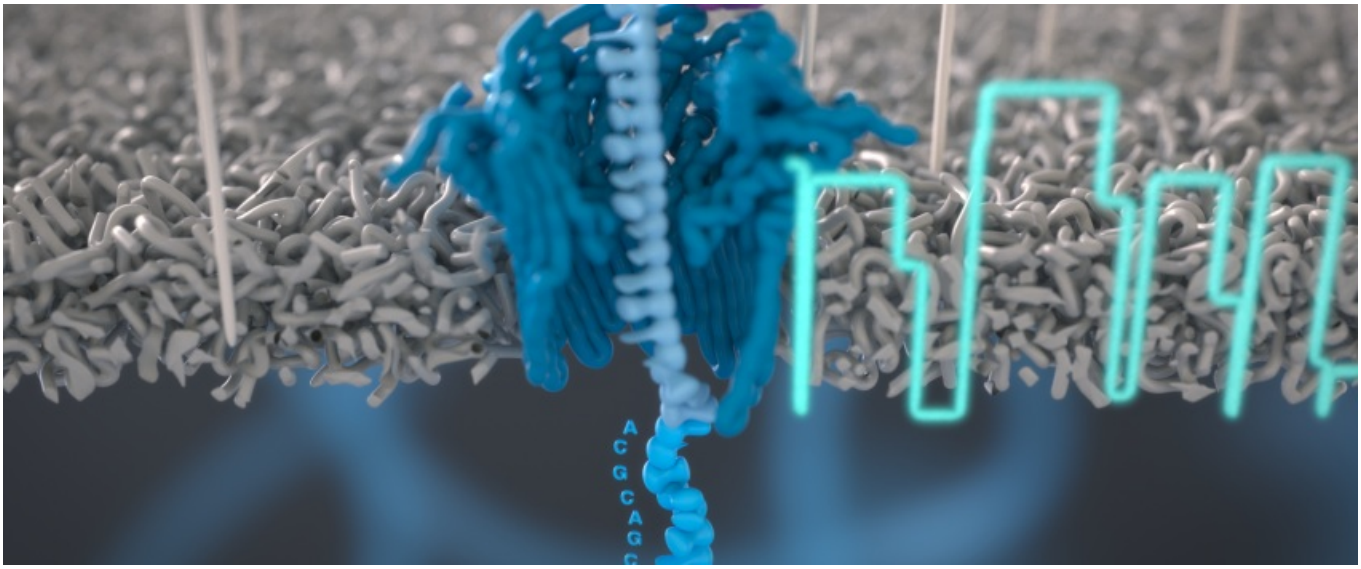
Evaluate Vantage

September 30, 2021

The heat is on for Oxford Nanopore

Elizabeth Cairns



Stock leaps in early trade, but to justify its huge valuation the technology might have to improve.

The 42% bump in Oxford Nanopore Technologies' shares on its first day on the London exchange means that the company's valuation is now further divorced from its sales figures than ever before. Its market cap sits at around £4.8bn ($6.5bn), despite sales coming in at just £59m in the first half of this year.

It will have to execute near flawlessly to justify this towering valuation. But, for Oxford Nanopore to take share from sequencing giants like Illumina and Pacbio in the lucrative liquid biopsy and prenatal testing segments, it is likely that three aspects of its technology will have to change.

Oxford Nanopore's tech works differently from the more established sequencing machines sold by all the big players in the sector. Nanopore's threads long strands of DNA through tiny holes in an electro-resistant membrane. As each base passes through it disrupts the electrical charge in a characteristic way; the change in the current over time thus corresponds to the DNA sequence.

90% of next-generation sequencing, including Illumina's technology, uses sequencing by synthesis (SBS). Fluorescent dyes attach to each base in a short strand of DNA, one by one. A camera detects the colour of each new label and builds up the sequence over time.

Oxford Nanopore's tech is faster than its rivals', and can sequence much longer strands of DNA. It also has an advantage in the cancer testing market in that it can perform epigenetic analysis of a patient's DNA simultaneously with the sequencing.

Epigenetic changes are chemical alterations to the bases, such as methylation, that can modify the activation of genes even though the actual sequence is unchanged; they are often have major implications for tumour development. Groups such as Illumina and Pacbio have to do epigenetic analysis separately.

The long and the short of it

But Nanopore's tech has three drawbacks. Historically it has not been as accurate as SBS: where that technology makes an error in roughly every 1,000 bases, so far Oxford Nanopore has not routinely been able to equal this. A spokesperson for Oxford Nanopore said that its sequencers can be more accurate than this under certain circumstances.

This could be about to change. Albert Vilella, a bioinformatics scientist who works as a contractor in the sequencing field, tells *Evaluate Vantage* that the group is close to perfecting duplex reading – decoding both

strands of DNA at once. SBS only works on single strands. Sequencing both DNA strands boosts the accuracy to the same level as SBS, he says.

This tech is in the process of being rolled out to customers under an early access programme, Oxford Nanopore says.

The second issue is price. Illumina can sequence a billion DNA bases for $6, whereas Oxford Nanopore's tech generally costs more for the same amount of data. A spokesperson for Oxford Nanopore says this $6 figure can be equalled with one of its technologies, and may be even cheaper if customers are on certain pricing plans or achieving higher throughputs.

The group will doubtless improve on price, but SBS tech is also getting progressively cheaper.

The final issue is to do with the length of DNA strands that can be read. Oxford Nanopore and a few other groups such as Pacbio offer long reads, producing sequences tens or even hundreds of thousands of bases long in one go. Illumina and most other groups do short reads – fragments 300 or so bases long that are later stitched together by a computer.

The trouble is, for the big-money clinical diagnostics segments like cancer screening using liquid biopsy, or non-invasive prenatal testing (NIPT), long-read tech is unnecessary.

These applications rely on sequencing cell-free DNA, drifting in the patient's – or in the case of NIPT, the mother's – bloodstream. And cell-free DNA is very short, Mr Vilella says, typically peaking at just 166 base pairs.

He compares using Oxford Nanopore's tech to read such short strands to driving a 4x4 vehicle around a city: expensive, and rather wasteful.

So, if the company is to try to take a slice of the blood-test screening segments, Mr Vilella says it will be necessary to make the technology more cost effective by developing a way to stitch short strands together before they go through Nanopore's sequencing machines. It is unclear how soon such a technology might emerge.

Priced for perfection

It seems, then, that a lot of conditions will have to be met for Oxford Nanopore to ramp sales high enough to justify its ballooning valuation. And there is very little wiggle room: even at the initial IPO price of £4.25 per share the company was priced for perfection.

Nanopore is forecast to have sales of around £93m in 2021, according to figures from sellside analysts shared with *Vantage* by a source. Revenues are predicted to reach £123m in 2022 and £170m in 2023. The group is modelling 2026 for Ebitda break-even.

If expectations are so low, why has the IPO been such a staggering success? The offering was partly derisked by a deal with Oracle: in mid-September the tech group had agreed to invest £150m at the same price as the IPO offer.

There is also a great deal of hype for a novel technology, not least because it has been used for Covid-19 testing (*The UK bets on Nanopore and Nudge for rapid Covid-19 tests, August 4, 2020*). London-based medtech and diagnostics IPOs are rare, and this scarcity may also have driven excitement. A sceptic might suggest that Oxford Nanopore's success could also have been helped by the fact that London has fewer biotech and medtech specialist investors than New York.

Lastly, of course, there is a great deal of enthusiasm for the biotech and medtech sectors, interest rates are low, and investors have to put their money somewhere.

One thing shareholders probably do not have on their radars is a takeover. Oxford Nanopore's unusual equity structure grants Gordon Sanghera, its founder and chief executive, a special class of shares with the power to block an unwanted takeover. Part of the rationale here could be to do with Solexa, the sequencing company taken out by Illumina for just $650m in 2007, and whose technology underlies Illumina's.

A takeover is still possible, of course, but seems unlikely in the short term.

Oxford Nanopore's insistence on remaining independent means that it will have to prove itself. When it closed its last funding round, a £195m raise in May, its post-money valuation was £2.5bn. One question for the market to ponder is: what has the company done to justify a step-up in valuation of more than £2bn in just five months?

This article has been updated to include comments from Oxford Nanopore.

More from Evaluate Vantage

Evaluate HQ
44-(0)20-7377-0800

Evaluate Americas
+1-617-573-9450

Evaluate APAC
+81-(0)80-1164-4754