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6 December 2019

Illumina / Pacific Biosciences Merger Inquiry
Comments for CMA Review from Customer and Industry Participant

To Whom It May Concern at the CMA:

I write this to provide comment on the proposed merger of Illumina and Pacific Biosciences, and to inform your review thereof with the perspective of a customer and third party participant in the genomics industry in which these companies both operate.

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Our products all use NGS sequencing as their key input good (thus making us customers of the NGS market), and companies such as ourselves are therefore highly subject to supply and competitive dynamics within the NGS market.

I should note that I composed the following observations entirely by myself, and that I have no legal training nor significant familiarity with UK merger law. However, I do have significant technical and operational knowledge of the NGS market. I believe there are particular features unique to the NGS market and its constituent technologies that are relevant to this merger and its likely effects.

I am cognisant of the raw amount of testimony and documentation already on hand in this inquiry, so I share here only a short sequence of thoughts, which are slightly technical in nature and may thus not otherwise be immediately obvious, but which I hope may be of use in your deliberations.

First: the Pacific Biosciences NGS platform is composed of multiple inter-related technical elements, which compound functionally in an 'exponential' manner to produce the analytic performance of their system overall. Thus: relatively small improvements in performance of individual such elements can lead to quite large increases in overall performance (e.g. output in gigabases), and likewise to quite large decreases in prices (e.g. price per gigabase). For example, output from any given 'chip' (e.g. the current Sequel II chip) correlates with the number of readable 'waveguides' on the chip, and also with the distribution of length and quality of DNA molecules successfully loaded onto the chip, and also with the distribution of actual readlengths (which itself is correlated with e.g. performance features of the polymerase, and with the optical systems used for sequencing).

Second: Pacific Biosciences has a long and consistent empirical track record of making such compounded, multi-element improvements in both customer prices and analytic performance for their NGS systems. This is true in terms of large, step-change improvements in prices and performance from the launch of new hardware systems (e.g. the Sequel and Sequel II systems), and in terms of further accretive improvements that have required no such major changes in hardware (such as the significant improvements in Sequel II output that have been achieved in the period following its launch, using only straightforward changes to the platform's molecular biology and related procedures).

Third: these exponential improvements in price and performance for the Pacific Biosciences platform are ongoing and show no signs of slowing, as evidenced empirically by the Sequel II launch itself and by the subsequent improvements in performance (and corresponding reductions in price-per-gigabase) following its launch. Furthermore, it is unreasonable to expect that – given this compounding effect – continued advancements in overall performance and reductions in per-gigabase prices of at least 10-fold/50-fold will not be achieved in the near term.

Specifically: it is likely that average readlengths will continue to increase by a factor of 4-8 in a 'hardware-independent' manner, as a function of ongoing improvements in sample preparation (resulting in longer and higher-quality DNA templates), improved sequencing polymerase enzymes and buffers, improved use/configurations of existing optical detection systems, and otherwise. It is also likely that the 'hardware-dependent' improvements will likewise continue, for example in the form of chips with larger numbers of waveguides and associated optical systems, which will also likely provide a further 4-8 fold improvement in near-term performance (for example, the Sequel II chip provided roughly an 8-fold increase in throughput, with a similar reduction in customer price).

Compounding these dimensions of quite likely improvements together, it would be unreasonable to expect less than a ~16-fold (4x4) to 64-fold (8x8) improvement in output from a Pacific Biosciences chip in the near-term future, with corresponding reductions in price-per-gigabase. As a commercial example, this would enable 30-fold whole human genome sequencing for an end-user price of ~$25-$100. And this is disregarding other potential physical and/or informatic improvements in throughput and/or accuracy, as well as further incremental cost enhancements from economies of scale in manufacture.

Fourth: In contrast to these significant and ongoing improvements being provided by Pacific Biosciences, Illumina has, by long-running and quite clear empirical evidence, almost entirely ceased improvements in price-per-gigabase over the past 5 years, due either to technical challenges, or to a lack of pricing pressure, or to some combination of both. Continuing from the above commercial example: the average price for whole human genome sequencing on Illumina products that is paid by individual end customers has remained unchanging at approximately $1000 for the past half-decade. One may suggest that this will only be changing coincident with the ongoing arrival of competitive pricing pressure from – for example – long-read NGS products supplied by Pacific Biosciences, beginning with the recent Sequel II launch.

Fifth: given these two long-running, consistent, unequivocal trends (exponential increases in output and reductions in price-per-gigabase for Pacific Biosciences products from hardware-dependent and hardware-independent improvements, compared with broadly unchanging price-per-gigabase for Illumina products), it is clear that the currently-nascent competition between Pacific Biosciences and Illumina is becoming rapidly more intense, and that the intensity and effects of this competition can only be expected to increase for the foreseeable future.

I appreciate that there are various legal standards and mechanisms for evaluating markets and competitive dynamics within them, all of which is quite beyond my understanding. And I appreciate that the DNA sequencing market is potentially challenging to analyse by traditional methods due to the radically dynamic nature of technology and pricing therein (e.g. as illustrated by the ~300,000,000% variance in price per human genome within the past 15 years).

But – and for what it's worth, as a lay-observer – it's quite hard for me to understand how these companies could be considered anything but direct current and future competitors, given the 'orders-of-magnitude' nature of NGS innovation, pricing, and customer purchasing. I appreciate that Illumina has historically out-competed Pacific Biosciences and other NGS providers, and at present still retains a small superiority on costs which has prevented larger-scale back-and-forth switching with long-read products. But tracking this cycle even just 12 or 24 months ahead paints a clear and intense competitive picture.

For example, I wonder the likely outcome if existing NGS customers were asked if, hypothetically (and as per the third point above), the existing Sequel II product were improved to have ~16-64 times its current per-chip throughput (i.e. providing whole human genome sequencing at $25-$100, or equivalently, providing any form of NGS sequencing for ~$0.30 to $1.25 per gigabase), whether they would consider substituting such a Sequel product for Illumina products, for whole genome sequencing and/or other various applications.

I suspect many customers across the NGS market would do so. And I suspect they would do so because short-read and long-read NGS products are fully interchangeable for the majority of NGS analytic tasks, and will be interchanged if and when and as such price points are allowed to emerge through the course of full, independent competition between these two large companies.

To summarise: Pacific Biosciences has finally entered a regime where its products are commercially competitive with those from Illumina, based on an enormous amount of sophisticated, sustained research and development compounded across its technology stack. And this competition can only be expected to increase in intensity and breadth in the near- and long-term future.

Sincerely,

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