

08 Feb 2022 | Interviews

Exec Chat: Illumina CMO Looks From Pandemic Boom To Future Where Genomics Is 'Foundational' To Health Care

by [Marion Webb](#)

Illumina's chief medical officer Phillip Febbo discusses expanding use cases for gene sequencing, the firm's planned introduction of new long-read sequencing technology Infinity, the status of its Grail acquisition, and additional plans for 2022.

[Illumina, Inc.](#)'s chief medical officer Phillip Febbo expects 2022 will be bright for the San Diego, CA-based gene-sequencing giant.

In an interview with *Medtech Insight*, Febbo pointed to new product launches, budding partnerships, double-digit revenue growth, and rising awareness of gene sequencing's vital role in predicting and diagnosing genetic disease as factors driving Illumina's confident outlook. (Also see "[JPM 2021: Medtronic, Biogen, Edwards LifeSciences, Guardant Health, Illumina](#)" - Medtech Insight, 11 Jan, 2021.)

Among Illumina's plans for 2022 is the rollout of a new long-read sequencing technology called Infinity, which will enable researchers to sequence about 5% of the genome that has thus far remained elusive for Illumina.

"We are taking all the appropriate measures to allay any concerns about this acquisition and creating a future potential anti-competitive situation." – Phil Febbo

Further, the CMO is confident that the shadow of regulatory intervention cast over Illumina's \$7.1bn acquisition of Grail multi-cancer early detection testing will lift.

In 2020, Illumina announced its acquisition of [GRAIL, Inc.](#), which develops the Galleri blood test capable of detecting more than 50 types of cancer. The acquisition was challenged by authorities including the US [Federal Trade Commission](#), which believes it would diminish innovation in the US market for multi-cancer early detection and boost prices. The [European Commission](#) objects to the transaction as well. (Also see "[Illumina Remains Committed To Grail Merger Despite Regulators' Doubts](#)" - Medtech Insight, 9 Aug, 2021.)

Illumina proceeded with the buyout in August 2021 despite ongoing regulatory investigations. The company said in the FTC proceeding, a third-party discovery issue has delayed the closure of the administrative record. It expects that issue to resolve this quarter and expects the judge's decision in the second or third quarter. (Also see "[Updated: Illumina Presses Ahead With Grail Merger Despite Antitrust Regulators' Opposition](#)" - Medtech Insight, 19 Aug, 2021.)



DR. PHIL FEBBO, CHIEF MEDICAL OFFICER OF ILLUMINA Source: *Illumina*

Illumina also said it would maintain both companies separately to comply with EU interim measures. On 3 February, the European Commission suspended the deadline for its review of the merger, which Febbo considers a "good sign" of engagement with Illumina's proposed remedies that address the Commission's concerns.

Febbo discusses below gene sequencing's current and future prospects, the importance of Infinity, developments around Grail, and what else lies ahead for the company.

Q Medtech Insight: In which clinical areas do you foresee the biggest opportunities for genome sequencing?

A Phillip Febbo: We've seen great value in genome sequencing for children suspected of genetic disease and now there's evidence about the validity, clinical utility, and the benefit to patients. We published a randomized trial in *JAMA Pediatrics* this past year that showed that use of whole genome sequencing in children with suspected genetic disease provides 50% more diagnoses. And in those with the diagnosis, the management changes 50% more often than if you delay that whole genome approach

and take more standard-focused approaches.

That study and many studies that have preceded resulted in many guidelines supporting whole genome use in genetic disease and moving towards meaningful reimbursement. It is a little disappointing that despite the evidence guidelines and reimbursement, there's still very little utilization. Only 5% to 10% of children suspected of genetic disease get early whole genome or any genetic testing. And that's something we're acutely focused on. Genome sequencing is moving also into understanding the impact of our own genetics on common diseases. Genetics will increasingly become important to all of our health and our health care.

Q Can you offer an example?

A Febbo: There are carriers that have dominant mutations in genes that can cause early cardiovascular disease, arrhythmia, heart failure, and increasingly we can identify those patients. In cardiology, we have a lot of treatments and lifestyle changes that can help decrease the impact of that. We also see the advent of polygenic risk scores [a single value estimate of an individual's genetic liability to a trait or disease] that look at small changes across many genes that can also markedly change the risk of an individual to early heart disease.

Finally, we know that the genome has variants [alterations in the most common DNA sequence] that affect how each of us metabolize drugs. The management of cardiovascular disease with the right prescriptions can be informed by genetics. We also have a lot of interesting information coming out about the genetics in dementia, autism, and other neurodegenerative diseases, and certainly metabolic disease with diabetes, liver disease, are really starting to gain some traction. I think the big movement of whole genome will move out of rare disease and into being foundational to our understanding of common diseases and people's risk to common disease.

Q In what ways is Illumina focused on driving increased use?

A Febbo: We at Illumina feel that there has to be increased awareness of the value of genetic testing for children suspected of genetic disease and for cancer patients who are determining therapy. We do also do non-invasive prenatal screening for pregnant women who want to understand the risk of their fetus having Trisomy 21 [Down syndrome] or other congenital genetic defects.

We've been building our own teams in our medical group that helped develop evidence, publish evidence, and also develop educational activities. We primarily work with the key professional societies to support them with information so that they're determining how to bring that to their members, whether it's pediatrics, neurologists, cardiologists or oncologists. There are incredible innovators out there that are using our platform to provide clinical tests. We're also developing in vitro devices to make it even more accessible. And as those become accessible, we want to also address the cost for patients.

Q Is cost the biggest barrier?

A Febbo: I think cost is a major barrier. You won't see meaningful adoption until there's meaningful reimbursement. Insurers have to make sure that these genetic tests are providing value to patients, are improving outcomes. They base those decisions on evidence and our team increasingly is engaging with academic centers, clinical centers, and directly with payers sometimes to generate the evidence to support those decisions. Today, there is growing reimbursement. If you look at reproductive health, cancer care and genetic disease, there are a billion lives that are currently covered in different geographies.

We still have a long way to go. In the United States NIPT [noninvasive prenatal testing] is covered for most women who are pregnant. Oncology comprehensive genomic profiling is becoming the standard of care and many public and private insurers are covering it. We are seeing that coverage included in the UK, Germany, and in France. I'm an oncologist, I'm used to taking care of cancer patients. It can't move fast enough, because I know outcomes do improve when you use genetic insight to manage cancer and other diseases. We're working very hard to accelerate as

fast as possible.

Q This year, Illumina announced plans to roll out a new technology called Infinity, which will read DNA in far larger chunks than before. Can you explain in layman's terms what it means to develop long-read DNA sequencing capabilities compared with short-read sequencing capabilities?

A Febbo: Short-read DNA technologies, like are presently available across our sequencers, cover the vast majority of the genome and cover it very efficiently, incredibly robustly. I've been very excited with what Illumina has been able to do with respect to bringing the cost down [and improving] the efficiency, the fidelity. The real workhorse of looking at a whole genome will remain those short reads.

But there is about 5% to 10% of the genome where the structure is hard to sequence and to understand the sequence of it with only segments that are 150, 250 base-pair long. You need segments that are a kilobase, two kilobases, 10 kilobases, because these areas have structural elements – they can be rearrangements, they can be duplications – that require those longer read segments. That's why we see there's incredible enthusiasm for short read to do most of the work, but also long read to get into some of those more difficult locations.

Q What does long-read sequencing allow researchers to do?

A Febbo: If you can imagine, there are areas that have repeated sections of sometimes just a few nucleotides, but sometimes large sections that are repeated. In those sections, there can be small changes, and in order to figure out how to position these repeats and reversions [which occur when the effects of one mutation are counteracted by a second mutation], you need to capture a longer piece.

There are areas like spinal muscular atrophy where the genes can be hard to deconvolute. There are also some genes that are involved in pharmacogenomics. Like CYP-2D6 is a gene that metabolizes a lot of drugs out there, there's a pseudo gene, and there are different alleles that can be very difficult unless you have a broader

perspective. We've been able to improve our bioinformatics to get to many of the alleles and to get almost complete insight in those two specific genes, but Infinity will really complete the process. There are technologies out there that can do de novo long reads [which refers to sequencing a novel genome where there is no reference sequence available for alignment]. But we also want to empower those with an Illumina sequencer to get to that information. Infinity has a special library prep process where we can empower Illumina users to get to those long reads in those regions that are more difficult.

Q Will long-read sequencing allow you to diagnose rare diseases or decipher parts of the genome that have remained a mystery?

A Febbo: It will help with that. What I anticipate is 90-95% of individuals who suffer from genetic disease, rare disease, can be diagnosed with short read. Because of efficiency and cost, that's likely to remain the first line test and it's incredible to see how quickly we can get to that information for children, for instance, in the NICU [newborn intensive care unit]. If an answer is not identified in that first pass whole genome, you can in the future reflex to run the Infinity assay to see if maybe you missed the diagnosis based on only having the short read. That's very much where we see the process going.

Q What is the cost difference between short-read versus long-read sequencing?

A Febbo: Right now, just the nature of the technologies, it's less expensive and more efficient and actually, the fidelity, the base pair calls, are higher quality with short-read sequencing. The challenge gets down to what are you comparing. Right now, you can get a high-quality 30x whole genome [30x means that your entire genome of 6 billion letters will be sequenced an average of 30 times] for about \$600 at Illumina. To get that same kind of 30x coverage across the whole genome it costs \$4,000 to \$5,000 with most of the long-read technologies.

Q What will it mean for existing Illumina customers when the Infinity technology will be launched?

A Febbo: It's incredible to see the growth in our business and how many customers we have, right? We have 20,000 instruments and more than 8,000 customers, globally. As Francis [deSouza, Illumina's CEO] articulated in the J.P. Morgan [Health Care conference] announcement, the pandemic has resulted in even more labs adopting our sequencing solutions across the globe. When Infinity gets released, those labs that are interested in looking at those more challenging parts of the genome that really require a longer read approach will be empowered to do that with these kits on the same sequencers.

Q One of your major competitors argued that 10 kb aren't long enough reads and that the challenge with this approach is that it's been tried several times and never really gained traction. How would you respond to this argument?

A Febbo: I think it all comes down to what's the question you're asking, as far as what's long enough. I am quite confident with this technology and the bioinformatics and our growing knowledge of genomic structure that 10 kb reads will address the majority of the challenging parts that are clinically relevant. As we roll this out, we'll certainly provide that evidence [and] a breakdown of what this library prep adds. It's not the same as a native long read and I'm looking forward to having that debate. Going from reads that are 150-, 250- 300- pairs to 10,000 is a meaningful change and will reduce the gap to very little, if any gap exists.

Q Can you provide an update on the ongoing investigation by the European Commission regarding Illumina's acquisition of cancer detection test maker Grail?

A Febbo: Grail is autonomous, and we've agreed to do that to respect the concerns and the process of the European Commission. We're continuing to follow through the process with the European Commission. We feel very strongly that this acquisition will speed the test [Galleri] to market and make it more accessible more broadly, more quickly, and save lives. Because of that, we are taking all the appropriate measures to allay any concerns about this acquisition creating a future potential anti-competitive situation.

The good news on agreeing is that the European Commission is looking hard at our remedies now and asking for a lot of information about exactly what the remedies are. We've put out a long-term supply agreement where we have real engagement with some of our key customers who are considering also participating in the multi-cancer early-detection market moving forward. It's going to be an incredibly important and competitive market. We're going to want to be the sequencing platform of choice for any company creating one of these tests. It's in our best interest to make sure that our acquisition of Grail does not decrease the enthusiasm that companies will have building towards a test.

Q What can you tell us about plans for 2022?

A Febbo: It's a super exciting year for us. We're also excited to see the launch of an IVD, TSO Comp [TruSight Comprehensive, a research-use-only pan-cancer assay that enables comprehensive genomic profiling from tissue biopsy samples], in Europe. Many of our pharma partners are excited to participate with an IVD in comprehensive genomic profiling. Our partnership with Nashville Biosciences is fascinating in that they have an amazing set of samples generated over the years with great clinical outcomes. (Also see "[JPM 2022 Mid-Week IVD Roundup: Guardant, Illumina, Ortho Clinical, Thermo Fisher](#)" - Medtech Insight, 12 Jan, 2022.)

When you combine really good understanding of diseases that individuals have together with genomic information in populations, it really gives you an idea to understand new potential therapies to improve upon outcomes. And we see a lot of customers investing in different databases, the UK Biobank activities, it's just going to be really exciting to see the insights that are generated over 2022. We're anticipating growth of 14% to 16%, another record year for us as far as revenue, and it's just a manifestation that genomics has always been fundamental to research but it's becoming increasingly foundational to health and health care. I think we'll continue to see movement in that direction this year.

Q Where do you see the potential impact of the ongoing pandemic?

A Febbo: Yeah, it's been a challenging time and certainly, we've worked very hard to minimize the impact of the pandemic on our customers with respect to maintaining consistent supply. We've had supply challenges as has everyone. We've been fortunate that most of our customers have had no drop in our supply. Sometimes we've taken longer to get them sequencers than we have in the past, but we've basically addressed that now.

On a broader scale, this pandemic has raised awareness of the importance of sequencing and understanding public health threats. It was the first time that my parents, who are both in their 80s, started talking to me about sequencing and variants. 'Doesn't your company do some sequencing?' Yeah, we do some sequencing ... I took that as a very good sign that it's starting to raise awareness.

I'm hopeful this 2022 will be a much different year with respect to the risk to all of us from this pandemic and the risk to society and our livelihoods. More customers have these sequencers in more parts of the globe. They're now going to ask what else can we do with this sequencer or what can we do for other infectious diseases like HIV, multidrug-resistant tuberculosis, malaria. What can we do for non-infectious noncommunicable diseases like heart disease, like diabetes, and cancer. I'm really excited to think about the opportunities to help those folks now transition to addressing other needs that are beyond the pandemic.