GenomSys Banks on MPEG-G Standard to Make Genome Analysis Mobile

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CHICAGO – GenomSys, a Swiss startup specializing in DNA data processing software, is preparing to introduce a variant caller and an annotation pipeline that will allow individuals to control and share their own genomic sequences with clinicians and researchers. The technology will be available both through a web portal and a mobile app for which the firm will pursue CE marking as an *in vitro* diagnostic tool.

A new CEO with digital health experience, Alessio Ascari, is guiding the Lausanne, Switzerland-based company through the launch.

While this is his first true job in genomics, Ascari, who actually joined the company in September, has a long history as a management consultant in digital health and therapeutics, most recently as head of his own consulting firm.

While Ascari was specializing in telecommunications and technology in an earlier role as a senior partner at McKinsey, mobile health became a hot topic after Apple upended the telecom world with the introduction of the iPhone in 2007. By 2008, Ascari created an internal program at the international consultancy called the Global mHealth Initiative, which brought together telecommunications, high tech, and healthcare to look for ways that new technology could improve healthcare delivery. Today, the field is commonly known as digital health.

"Every individual should be able to control the use of his own DNA," he said. "This is what we call bringing privacy and convenience of analysis to the individual."

Today, DNA generally is stored out of the immediate control of the individual and in some countries, the data is sold.

"A lot of people make a decent business around leveraging this amount of data, selling it to pharma companies for genomic research," Ascari said. "That is not wrong *per se*, but we believe that protecting the privacy of the user for the most precious data should be paramount."

"Our vision is really to enable people to consent on this research use of their DNA on a case-by-case basis," Ascari said.

type of platform in genomics, either. Companies including Ciitizen, LunaDNA, Seqster, and E-Nome are all offering or developing similar concepts.

Ascari acknowledged that building a market will take time, perhaps years, but said that the chance of success is higher in genomics because the field hews more closely to data standards than does the EHR market. He also noted that EHRs originally were created to facilitate billing rather than diagnostics and patient care, and even today often are hospital-specific or laboratory-specific.

For its part, GenomSys is banking on the MPEG-G genomic data compression standard to support its technology and business plan. This is the genomics version of the MPEG — which stands for Motion Picture Expert Group — that brought the world the MP3 format for digital audio and MPEG-4 specification for compressing video files.

Among other things, MPEG-G promises to give individuals access to genomic data and other aspects of personalized medicine on mobile devices.

During a Zoom call with GenomeWeb this week, Ascari showed a prototype proof-of-concept app that held a compressed exome file and performed variant calling in just a minute or two on his iPhone 12, Apple's most current model. He said that an iPhone 6s or 7 from several generations ago could also process this data, though at a slightly slower pace. An Android version also is in the works.

"The variant calling is run directly on the phone, extracting the data from the file on your phone, processed on the phone, and only at the end the VCF file could be shared in the cloud for annotation and reporting by an accredited physician," Ascari said. The physician is necessary to assure that the result is of "diagnostic quality," he added.

The pipeline that runs on a phone is identical to one that GenomeSys hosts in the cloud for those who want to access the technology from a computer. Ascari said that both the pipeline and the app will be ready for public release in the second quarter, though the pipeline probably will be done first.

GenomSys Cofounder and CTO Claudio Alberti was heavily involved in creating the MPEG-G standard. The International Organization for Standardization (ISO) formally approved MPEG-G in 2019 as ISO 23092.

In a 2018 preprint article that Alberti was co-first author of, the MPEG organization and ISO said that the new standard addresses the issue of "efficient and cost-effective handling of genomic data by providing not only new compression and transport technologies, but also a family of standard specifications associating relevant information in the form of metadata." They said that MPEG achieves 10x compression gains over the BAM file format.

With MPEG-G compression, a whole-exome sequence needs just 1.5 gigabytes of storage, making it easily fit on a modern smartphone, according to Ascari. He said that a whole genome might take up 10 to 15 GB, though current iterations of GenomSys software have not attempted to process whole genomes yet. "We can run the variant calling directly in the phone thanks to the efficiency and the selective access of the standard," Ascari said.

Ascari said that MPEG-G offers three advantages: efficient compression, a high level of encryption, and "selective access." The latter, he said, means that a researcher or diagnostician would not have to extract the entire genome, exome, or chromosome to look at specific genes, providing privacy and speed gains, and sometimes even cost savings on analytics and computing time.

However, MPEG-G has been met with skepticism by some who believe that the Global Alliance for Genomics and Health (GA4GH) is the best standards-setting body for the bioinformatics world. This was the subject of some lively debate at the 2019 Intelligent Systems for Molecular Biology and European Conference on Computational Biology (ISMB/ECCB) conference in Basel, Switzerland, just a few months

before ISO formalized the 23092 standard.

Around the same time, GenomSys raised CHF 9.3 million ($10.2 million) in a Series A investment round.

Ascari noted that GenomSys is a member of GA4GH, and said that potential partners and adopters of MPEG-G have expressed interest in the fact that it is an ISO standard and that the specifications are "open, clear, and public," not tied to any one company or group of companies that may someday go out of business.

"It's future-proofing your investment," Ascari said.

Ascari said that for the first three-plus years of the company's existence, the focus was on developing and seeking approval of the MPEG-G standard. About a year ago, the shift into app development began in earnest.

The new GenomSys variant caller and annotation pipeline will operate "natively" with MPEG-G files, according to Ascari. Because older standards area in wide use, GenomeSys has created transcoding tools to convert other files into the MPEG-G format.

GenomSys already is collaborating with laboratory software developer SysMeta IT to implement MPEG-G at clinics and labs in Switzerland. SysMeta IT is integrating GenomSys' MPEG-G tools into its Tangerine Medical software for viewing and annotation of patient records and for electronic ordering of sample analysis.

The ideal scenario for Ascari is for GenomSys to support precision medicine. "You go to the doctor, you start talking about some medication, and you can check on the phone almost in real time or have your doctor check on the phone in real time what is the impact [of the drug] based on your genomic data," he said.

While this kind of workflow remains a future hope for Ascari, he said that MPEG-G makes this technically feasible now, even if software and human behavior haven't quite gotten there yet.

GenomSys sees hospitals and labs as its primary customer base. In this sense, Ascari said that the company is not trying to be disruptive or revolutionary.

"We are just bringing the benefit of the MPEG-G standard to the current processes. We don't want actually to revolutionize the processes of the lab" he said. "We want to improve the level of efficiency without the changing the way geneticists work."

Expect the Swiss company to concentrate on Europe initially, but Ascari does want to explore other markets including the US "very soon," perhaps with the help of partnerships. called the US an important market that "we will definitely also consider."

Makers of *in vitro* diagnostics products have until May 2022 to comply with new European Commission regulations. Ascari said that GenomSys expects to meet those standards before the deadline.He said that gaining regulatory approval or clearance in whatever jurisdictions the company sells in will help GenomSys boost market confidence in its products.

"Our purpose is to bring personalized medicine and genomics really closer to the individual, but with a high protection of privacy," while also supporting clinical quality, Ascari said. "We really want to do everything that we can [so] this can be applied for diagnostic and treatment in compliance with whatever regulation is in specific countries.