



Startup Resolve Biosciences Readies Launch of Spatial Gene Expression Analysis Service

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NEW YORK – Resolve Biosciences, a company formed by several former Qiagen executives including former CEO Peer Schatz, is planning to offer services on its new high-resolution spatial analysis platform in early 2021.

The German firm, which emerged from stealth mode [last week](#) with a \$24 million Series A financing round, hopes to get an early-mover advantage in the targeted, highest-resolution side of the rapidly bifurcating spatial analysis market by offering its single-molecule fluorescence *in situ* hybridization (smFISH) and imaging technology. Resolve's "Molecular Cartography" offers spatial resolution of .27 micrometers, around the diffraction limit of light — enough to resolve single cells and even subcellular patterns of gene expression, CEO and Cofounder Jason Gammack said. Transcriptome-wide, but lower resolution technologies are more mature and offer complementary features to Resolve's technology.

"It's completely novel chemistry," Gammack said. A front-end sample preparation protocol fixes fresh-frozen tissues or cultured cells to a slide, which then goes through cycles of automated probing, colorization, and imaging.

For now, the technology will offer insights into gene expression patterns, but Resolve plans to add DNA, protein, and even metabolite analysis in the future. The method preserves tissues for re-analysis and offers spatial information in 3D. After launching its services in the first half of next year, Resolve plans to develop instruments for core labs, and, ultimately, individual labs.

An early-access program, launched about a year ago, has already produced data for customers in both pharma and academic research. Resolve's platform "hits the sweet spot between multiplexing capability, sensitivity, and resolution," said Michiel Bontinck, a life science technology specialist at VIB Tech Watch in Belgium, an early-access customer. VIB Tech Watch evaluates new technologies for a consortium of six Belgian research institutes and has experience with other spatial gene expression technologies. "You can do a lot of things with it: bottom-up research, validation of single-cell RNA sequencing experiments," he said.

"The data we've gotten so far is very impressive," VIB Tech Watch's Jeroen Aerts said, adding that this was due to a high probe-capture rate. "Resolution and sensitivity are what we really highly value in this tech," he said, noting that Resolve's platform achieved subcellular resolution.

Resolve is keeping a tight lid on performance and other details of its platform for now. Gammack declined to discuss pricing but said the technology will be "priced competitively to technologies in the marketplace." VIB Tech Watch members said they were not allowed to discuss performance metrics, either alone or in comparison to other platforms.

Gammack declined to describe the proprietary aspects of the firm's chemistry, including how it designs and manufactures probes. "When we go to market next year, we're not going to market with a beta technology," he said. "We're going to market with something that has been battle hardened."

Resolve's origins lie in Gammack's time at Qiagen, where he was a VP in charge of global commercial operations. Sometime before 2016, he evaluated the life science research market to find areas for strategic growth and identified spatial analysis as a prime target. "There are many unmet needs and some real opportunities," he said. Qiagen began developing spatial analysis technology in 2016, Gammack said. But in 2018, he left Qiagen to become chief commercial officer at Inscripta, a firm offering [the Onyx gene editing platform](#), while Qiagen continued developing the technology. In late 2019, Schatz offered him the chance to start a new business around that spatial technology, including seeking new funding. "Money flows where opportunity exists," Gammack said.

Resolve will use the \$24 million it recently raised to develop the platform and to build operations in California, enabling it to service North America. The company currently has 35 employees at its headquarters in Monheim am Rhein, Germany, and plans to grow by bolstering both R&D and commercial staff. Gammack said the firm is placing much emphasis on bioinformatics. Approximately one in four employees are working on the computational side of the platform, he said, including image analysis, "hardcore bioinformatics," and computation. Finding the right facility in California has so far proved a challenge. "Lab space is a little tough to find these days with everyone spinning up a coronavirus test lab," he said. The firm is also eyeing expansion into Asia.

Resolve is entering the high-resolution spatial analysis space at the tail end of a year in which competitors have mushroomed. [Vizgen, a Harvard University](#) spinout commercializing multiplexed error-resistant fluorescence *in situ* hybridization (MERFISH) technology, launched an early-access program this year. Also, 10x Genomics, which already offers the lower-resolution but whole-transcriptome [Visium](#) spatial transcriptomics platform, [acquired ReadCoor's *in situ* analysis platform](#) as well as Cartana, a Science for Life Laboratory (SciLifeLab) spinout offering kit-based *in situ* RNA analysis. And earlier this month, NanoString Technologies announced to investors that it is developing [a high-resolution spatial analysis platform](#) to complement its GeoMx Digital Spatial Profiler, that will be accessible next year and fully launched in 2022. And late in 2019, the SciLifeLab researchers who developed the spatial transcriptomics method underlying Visium described a new [high-definition spatial transcriptomics](#) method that claims 2 micrometer resolution.

As previously estimated by NanoString CEO Brad Gray, the spatial analysis market could be worth \$12 billion or more, about half of it addressable by high-resolution technologies capable of resolving cells or subcellular structures. Gammack said those figures were "not unrealistic" although a lot depends on how one defines the market.

As its name suggests, resolution is where the company hopes to differentiate itself. "Our ideal customer is one that has a hypothesis and wants to validate and iterate on that hypothesis," Gammack said. Researchers looking to analyze 50,000 genes at once should probably turn elsewhere, he suggested. Resolve's platform should be able to analyze hundreds of genes at once, with early-access customers currently analyzing between 50 and 200 genes. "I think that will scale, as the technology and data analysis matures," he said.

But the firm offers molecular information across the whole slide. "You have the wide view where you can look at thousands of cells and you can zoom in and look at subcellular structures," Gammack said.

Probe sets will be customizable, though the firm already has preconfigured probe sets, based on commonly interrogated genes. "But there's no limitation to design [probes] against a gene we haven't detected previously," Gammack said. Resolve has used the technology on tumors and several major tissue types, including those from the human brain, kidney, liver, and lung.

Being able to work with formalin-fixed paraffin-embedded tissues "is on our roadmap," Gammack said. "It's very challenging and not all FFPE is created equal." The firm has also investigated using [Paxgene](#)-preserved tissues, an FFPE-like method developed by Qiagen.

Gammack noted that while some software will be proprietary, the firm also hopes to encourage open-source development. "We want to make sure our datasets are available to be analyzed and well annotated," he said.

So far, Resolve has six early-access partners, three in pharma and three in the academic research market.

"We have a good connection with them," Bontinck said. "They take the input from VIB very well." Researchers at VIB work with many different sample types, which has made the institute a demanding partner. "From their perspective, it's never 'That's impossible, we won't try it,'" he said. "Their first reaction is, 'Let's try it.'"

One research project at VIB used Resolve's platform to complement single-cell RNA sequencing data coming from 10x's Chromium platform for the analysis of mouse hippocampus. Another, also analyzing mouse brain, tracked different cell subtypes throughout development. "This is very sensitive technology that allows us to look at low-expressed genes," Aerts said.

In addition to human and mouse samples frequently found in the translational research field, Gammack said the ag-bio market is showing interest in applying the platform to plant tissues. Diagnostics is another application that can't be ignored, he added.

"We want to help improve healthcare," Gammack said. "But we're not developing any clinical applications now. That's well down the road."

"We need to understand where it can be applied" in fields like oncology and immunology, he said. "It's not clear to me today what those clinical use cases are. But I am very confident that, in time, those clinical use cases will be developed and they will have significant diagnostic yield."