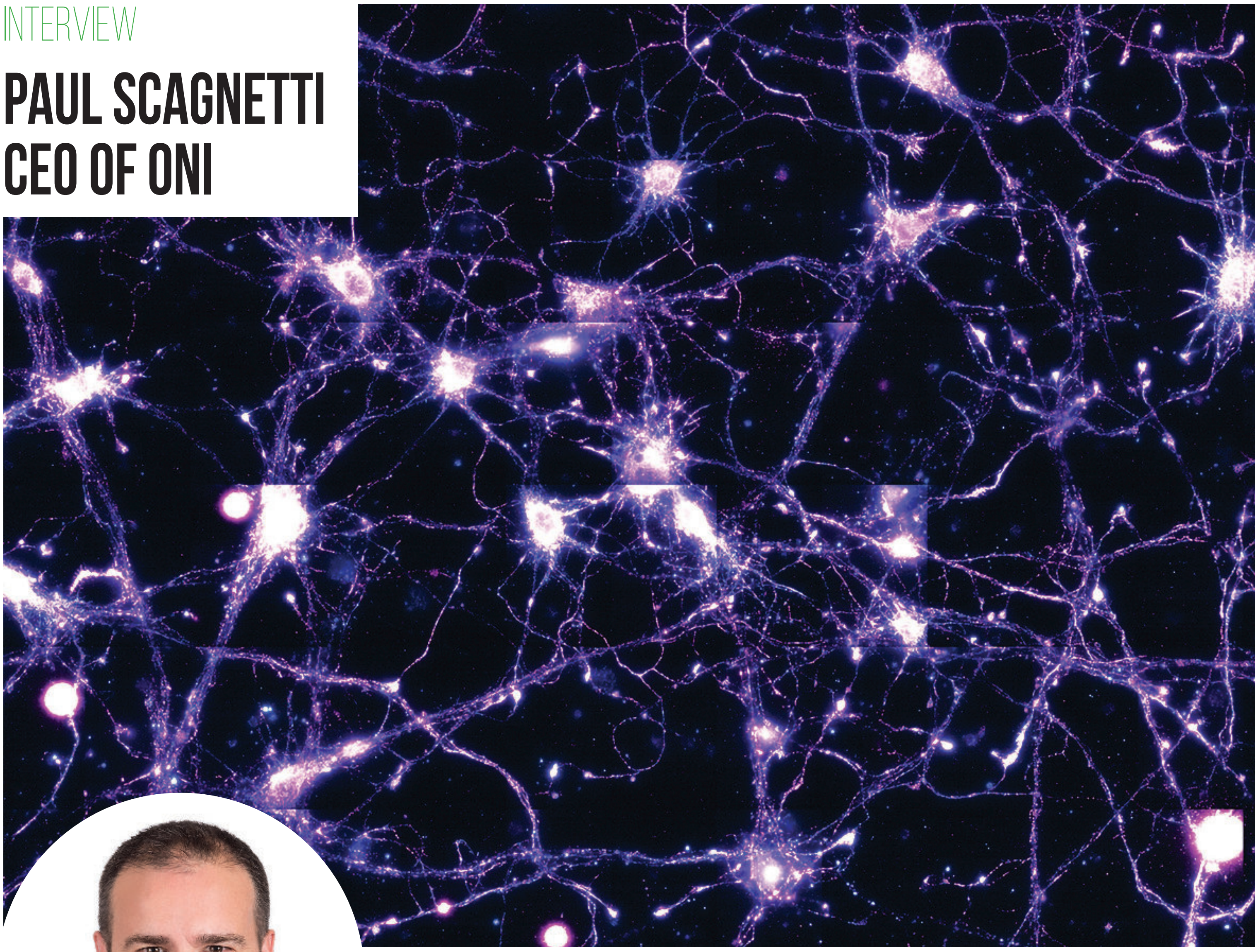
INTERVIEW

PAUL SCAGNETTI CEO OF ONI



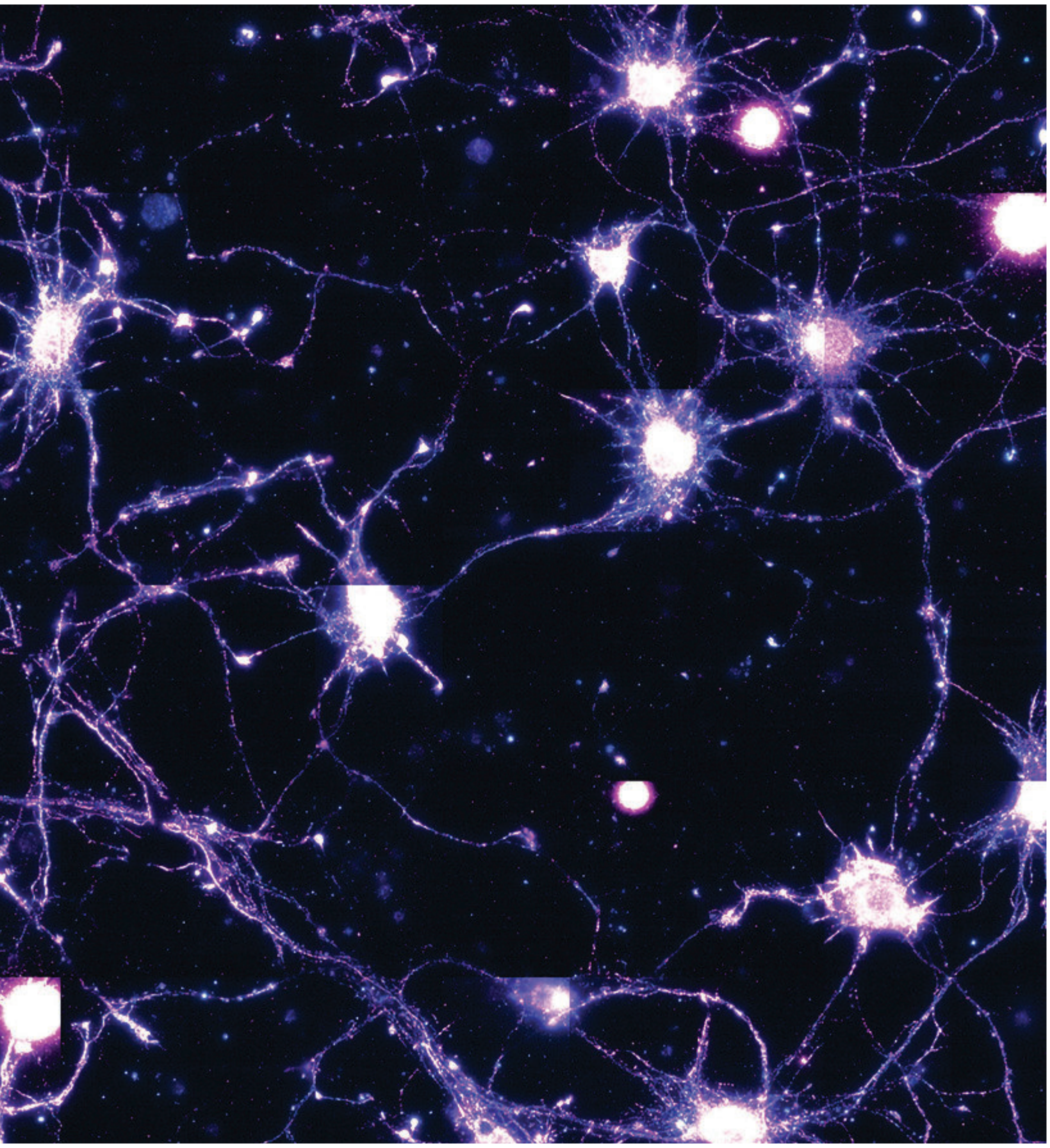
Paul Scagnetti is the visionary CEO of ONI, a groundbreaking technology company renowned for its cutting-edge super-resolution technology. With a robust foundation in artificial intelligence and deep roots in Oxford, Scagnetti has positioned ONI at the forefront of technological innovation.

Scagnetti's journey into the tech world began with his academic pursuits at MIT, where he earned his PhD in mechanical engineering. His time at this prestigious institution not only provided him with a solid technical foundation but also exposed him to a network of leading researchers and innovators. This environment fostered his interest in artificial intelligence, ultimately guiding him towards developing transformative technologies.

Under Scagnetti's leadership, ONI has made significant strides in the field of super-resolution imaging. The company's flagship innovation, the Nanoimager, exemplifies Scagnetti's commitment to pushing the boundaries of what is possible. This advanced imaging technology offers unprecedented clarity and detail, revolutionizing fields within scientific research. By leveraging AI, super-resolution can analyze images in real-time, providing insights that were previously unattainable.

Scagnetti's strategic vision extends beyond technological development. He has cultivated a corporate culture at ONI that prioritizes innovation, collaboration, and ethical AI deployment. His leadership style emphasizes continuous learning and adaptability, ensuring that ONI remains agile in the fast-evolving tech landscape. Scagnetti is also a strong advocate for responsible AI, emphasizing the importance of ethical considerations in the development and implementation of new technologies.

Through his work at ONI, Paul Scagnetti has demonstrated a remarkable ability to blend technical expertise with visionary leadership. His contributions to AI and super-resolution imaging are not only advancing the industry but also setting new



standards for innovation and ethical responsibility in technology. With the company's deep roots in Oxford and a forward-thinking approach, Scagnetti continues to steer ONI toward a future where technology and humanity progress hand in hand.

How do you see ONI's super-resolution technology evolving to support advancements in personalised medicine and pharmacogenomics?

The important thing to understand about what we do is we help people see molecules interacting in real time and in the site of the interaction. And so if you think about it, your cells and most of the things in your body are ultimately made up with molecules. And it has historically been very difficult to observe interactions at that level. And in particular with interactions, what we do is enable therapeutic discovery by helping people see through previous blind spots.

And so what we mean by that is, with a regular microscope, you can observe cells and tissues, but not individual molecules. We enable that level of detailed observation with far greater simplicity than the alternative methods.But a lot of cellular structures ultimately break down to things that are in the nanometer scale, which is almost an unfathomably small scale of things. And so things like the antibodies that are associated with fighting disease in your body are also a means of delivering drugs. If you look at viruses, if you look at the way that, for example, the COVID vaccine that many of us took, they've packaged mRNA into a lipid particle. And those particles are typically in the 50 to 100 nanometer range.

Basic microscopes can't reach this level of detail. Even high-power, non-super-resolution microscopes can only show cells and organelles. To watch a COVID vaccine particle with mRNA entering your cells, traditional microscopes fail; it's a blind spot.

You might know that the COVID vaccine contains mRNA and you can monitor the tissue's response, but our tools allow you to visualize the entire movie of the vaccine's journey into the cells. And so that's the fundamental thing that we do. It's important when you are trying to understand exactly what the process is, so that you could make vaccines or drugs that are very specific to the cells you want to target, or even to sites within a certain cell.

Your Nanoimager platform has made super-resolution microscopy more accessible. What breakthroughs in life sciences do you anticipate this democratisation of technology will enable?

A lot of them will be associated with therapeutic discovery, as the main area, but there will also be new biomarkers that we find, for example, new proteins that participate in a process and can be targeted by drugs. I think fundamentally these are the two biggest areas where we will enable pharmaceutical companies to develop better therapeutics.

And then we'll enable diagnostic companies to find better, more precise diagnostics, so that when people are dealing with a particular disease state, they'll have better diagnostics. These advancements in therapeutics and diagnostics are the two biggest areas where we can make a significant impact.

How is ONI integrating AI and machine learning into its imaging systems, and what impact do you foresee this having on drug discovery processes?

There are two ways. In one sense, people often divide AI into generative AI and then machine learning. So in the near term, the most obvious way is through machine learning. When you look at things that are at the scale that we're at, they're so small, that you have to look at gigabytes, and gigabytes of data to have a sense.

You don't want to just watch one particle of a therapeutic molecule being up-taken, you want to watch that a million times, and then make some sense of it and distill that. And so, one way is to synthesise a lot of information and to pull out the bits and pieces that are the most important for a researcher doing discovery work.

The other way is through generative AI. I think that there is going to be a combination of different techniques that are going to put together molecular movies effectively — which will be based on super-resolution and also known structural information of the molecules.

I think in the very near future, you'll be able to see almost as though you were a molecule. You'll be able to shrink yourself down and watch molecules interacting and get a generated molecular movie animation of what's happening with a molecule entering the cell.

And not just an animation — like a pretend thing, but a real thing that is showing a real mechanism of action. So I think it's going to be twofold. In terms of the way AI, super-resolution and other molecular techniques come together.

ONI has roots in Oxford but has expanded globally. How are you leveraging international collaborations to drive innovation in super-resolution microscopy and beyond?

The best thing that we have in our business is that we sell to both leading academic researchers and we sell to biopharma companies. So one of the most fun parts of our job is that we deal with academic researchers at leading universities and many of those leading universities have our microscopes.

And then we deal with the pharma companies and they each want slightly different things. The academics want to develop methods and want to do fundamental discovery. The pharma companies are doing it for purposeful, more targeted application specific discovery — for the purpose of discovery and new therapies.

And so you could picture it as a triangle, sometimes where we're providing a technology, we provide it to the leading academics, and then those academics also work with pharma companies, and vice versa. So that's one way to think of how this works. We are global, and we're working with both the academic researchers, and also pharma researchers, but we are all on the same team and we are excited to hear about the discoveries that scientists make using our products.

What has been the main barriers to drive overall adoption of super-resolution in research and discovery?

The main one has been that it's complex to do molecular scale imaging. And that's true. In any area where a new life science tool technology comes in or a new discovery tool comes of age, it's always extremely valuable, but a little finicky to use.

And so one of the challenges in our case is getting the chemistry, the

software, and the hardware to all work in unison — in a way that's easy and consistent for researchers. And that they get consistent results day after day.

And so if you and I were to go into the lab today, and to try and get a result, it would be substantially less time than it would have been two or three years ago, to get a single super-resolution image.

So really, it's been about simplifying and making the technique more consistent, more foolproof, easier, and more accessible to people who don't have all the time in the world to study a particular technique and want to use the technique to get a result. So I think ease of use and a sort of bullet proofing have been two of the biggest things that have been barriers to adoption.

What are the blind spots that you believe exist in current drug design which super-esolution can help reveal?

I think it depends on the particular type of therapy. But in general, one of the biggest blind spots is what people refer to as a mechanism of action, which means how exactly is a therapy being up-taken and working in a biological system with cells.

And so that general blind spot plays out in different ways, whether you're looking at antibody based therapeutics, and there's a couple different flavours of those antibody drug conjugates by specific antibodies. Then the same thing on drugs that are packaged into, say, lipid particles.

Even though we often see the effect of drugs, the biggest blind spot is understanding how exactly they are up-taken into the cells. That's one of the main things that we work on with customers. We see it as our job to give people a new kind of camera into the molecular world.

Again, our goal is to enable researchers to go beyond just observing the end states, such as 'I put this chemistry in' or at the macro scale, 'I see this result in a patient.' We want them to actually see down to the level of molecular interactions and watch what is happening in real-time.

With the increasing complexity in drug design and biological manufacturing, how could you see ONI's technology contributing to make manufacturing more efficient and safer?

Once a company has discovered a molecule and discovered that it works; whether it's an antibody, whether it's a lipid nanoparticle that's packaging RNA, or something else; the question then becomes when they're manufacturing, how consistent is what they're manufacturing, whether it's a set of antibodies, a set of lipid particles — how consistent are those relative to the intended molecule?

And super-resolution is one of a multitude of technologies that is capable of giving people that quality control of saying, "Hey, this is what we intended." Now, let's take a sample out of the large batches that are being manufactured, and see if those are consistent with what we developed in the clinical trials.

So that's the conceptual link in the way that we contributed. We're not the only technique, of course—there are many others. However, we can help companies examine large batches of manufactured products and compare them to what was used in earlier stages of research.