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# PROFILING PROWESS FOR PRECISION CANCER CARE

A conversation with **DAVID SPETZLER**, Chief Scientific Officer at Caris Life Sciences

Caris Life Sciences is the world's largest and oldest molecular profiling company for cancer, analyzing tumour samples for cancer biomarkers in the form of DNA, RNA, and protein aberrations. In February 2019, the company added a test that increased the number of searches for RNA abnormalities from 53 to approximately 22,000 genes. Caris' advanced AI platform uses these data to clarify treatment options, producing high-quality information within the necessary timeframe.

**How is the service provided by Caris Life Sciences unique?**
We've been profiling tumours since 2009, conducting approximately 2.5 million tests, so we draw on an immense dataset to conduct sophisticated analyses of patient samples. While there are overlaps in molecular alterations within and between cancers, the physiology and lifestyle of each person means that every tumour has a subtly different molecular signature. These tiny differences mean that a drug might work very well for one patient, but has side-effects, or no effects, in another. It is our goal to provide biomarker diagnoses and treatment advice for oncologists about every person they treat, regardless of the type of cancer, using our proprietary algorithms like the Caris Molecular Disease Classifier. There is no 'one size fits all' approach — tailored, precision treatments are vital to fight cancer.

**How does your molecular profiling system work?**
Our Caris Molecular Intelligence® platform comprises multiple, rigorous tests to build a comprehensive picture of alterations in tumours that we can trace to identify different cancers and their subtypes. Our goal is to determine what is driving the growth and progression of every tumour to identify the most relevant therapies for every patient. We use a 592-gene DNA panel to help us scan through thousands of potential mutations, while our unique proteomics technology, the ADAPT Biotargeting System™, looks for subtle protein changes. This year, we introduced MI Transcriptome™, whole transcriptome sequencing that allows us to look at approximately 22,000 genes and pinpoint RNA variants and RNA changes caused by fusions between genes, hallmarks of certain cancers. We now have the most extensive catalogue of cancer biomarkers in the world.

**How do you pinpoint drugs that may work for individuals?**
Our AI platform, DEAN (Deliberation Analytics), helps us combine our molecular dataset with another dataset of clinical outcomes. For every biomarker, we have data on other patients, what drugs they were treated with, and their outcomes. DEAN learns from these data, and uses non-linear feature selection to find relevant associations in the vast informatic space that our profiling generates. DEAN identifies signatures that help predict which patients might respond to specific treatments; a process known as Next Generation Profiling™.

## THERE IS NO 'ONE SIZE FITS ALL' APPROACH TO CANCER.

We also conduct extensive searches through the literature and clinical trial records to match individuals to the best possible treatment options. If a new drug is being trialled targeting a specific biomarker, we may recommend a patient for that clinical trial.

We also highlight drugs that would be ineffective given the molecular make-up of a tumour. This narrows down treatment options, making oncologists' decisions easier, and reducing the risk of adverse reactions, or the stress of undergoing treatment that fails. This streamlines cancer care and makes it more cost effective. In terms of costs, we work closely with US health insurance companies to ensure our services are covered for as many patients as possible.

**Can you screen most solid tumour samples, even if they only contain a small amount of cancerous tissue?**
Yes. We've developed a unique microdissection method to analyze samples that have a low percentage of cancerous cells. For an assay to work, a sample needs at least 20% of cells to be cancerous. Some tumour samples have only, say, 15% cancerous cells, but they are concentrated within a small tissue section. We carve out that section; within it perhaps 50% of the cells are cancerous, so we use that to build the profile, and have a 95% success rate.

**The data you have collected contains invaluable information. Do you share data with other research groups?**
Absolutely. It's important that oncologists and patients know that their data is available to them for scrutiny. Further, anonymized data is shared widely with scientists and mined for information – we've set up the Precision Oncology Alliance to help us work closely with researchers globally. Essentially, we have a continuous feedback loop between finding new biomarkers and interpreting their significance, providing insights for drug developers which ultimately feed back into our system and directly helps patients. We also have strong links with Arizona State University, where our employees can study for a PhD, paid for by us, to contribute to our research.

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