

Caris Life Sciences

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Powering the future of precision oncology medicine with big data

By combining molecular science and artificial intelligence with years of experience and a world-leading database, Caris Life Sciences aims to revolutionize cancer care and deliver on the promise of precision oncology medicine in partnership with biopharma and industry innovators.

Imagine a world where every cancer patient can hear the words: “don’t worry, we have a personalized treatment that can help your type of disease.”

Caris Life Sciences, headquartered in Irving, Texas, is focused on making that possibility a reality. Caris is a precision medicine company that uses whole-exome DNA sequencing (WES) and whole-transcriptome RNA sequencing (WTS) to understand the biology of diseases and optimize patient-centered cancer-treatment decisions.

Over the last 15 years, Caris has developed one of the world’s largest databases comprising over 455,000 patients’ genomic profiles, along with clinical outcomes and digital pathology. The majority of these profiles include WES and WTS of more than 20,000 genes, typically yielding more than 1 TB of biomarker data per patient. The depth of this ever-growing cache of clinical data enables insights that not only help patients today by informing optimal treatment decisions, but also allow Caris to partner with biopharma companies to guide development strategies for the next wave of therapies (Fig. 1).

Reinventing precision oncology

Each patient and each cancer diagnosis is unique, and may respond differently to a therapy.

“Tailoring therapy to those patients who are most likely to benefit—while sparing unneeded exposure and toxicity to those who will not—is the underlying tenet of precision medicine,” said Milan Radovich, Caris’ chief precision medicine officer.

Caris’ comprehensive precision medicine approach to assessing DNA, RNA and proteins is underpinned by a belief in good specimen stewardship. According to the company, sequencing all genes not only yields far more biomarker data from often limited specimen material, but also the power of such comprehensive information in aggregate can be deployed to improve patient outcomes today and in the future. The breadth and depth of data make Caris’ methodology fundamentally different from the currently available panels, which are limited by only looking at known biomarkers.

“Limited panels go out-of-date as new drugs with new biomarkers are found, and as our understanding of cancer evolves. These smaller panels also mean that researchers can find only the currently known disease biomarkers and drug associations. In contrast, comprehensive profiling means that researchers can look beyond known biomarkers and into the unknown to find new signatures and patterns,” said Caris’ president and CSO David Spetzler. “By getting the

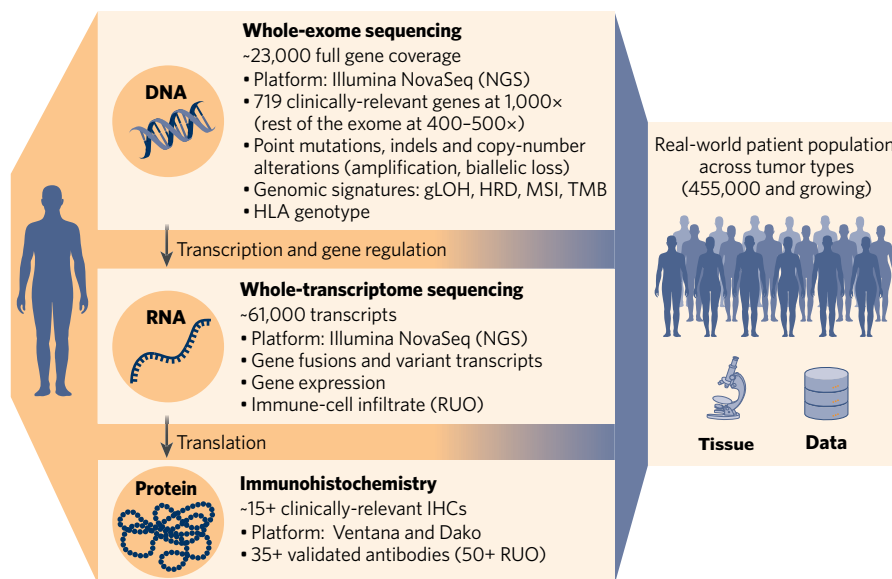


Fig. 1 | Caris’ comprehensive platform fuels biopharma solutions. Caris’ comprehensive approach to point-of-care patient-level profiling to guide treatment decisions today has also fueled the growth of an unmatched population-level tissue repository and clinico-genomic database that can be leveraged in partnership with biopharma to inform and optimize treatments of tomorrow. gLOH, genomic loss of heterozygosity; HLA, human leukocyte antigen; HRD; homologous recombination deficiency; IHC, immunohistochemistry; MSI, microsatellite instability; NGS, next-generation sequencing; RUO, research use only; TMB, tumor mutational burden. Real-world patient population correct as of February 2023.

most out of every sample, comprehensive profiling supports the advancement of science and ensures the relevance and actionability of the information for each patient sample over time.”

For Caris’ biopharma partners, this results in actionable insights that can help identify patients for approved therapies or clinical trials and optimize development strategies. It also means that

Caris’ database is a treasure trove for biopharma seeking to discover new cancer vulnerabilities, drug targets, and predictive biomarkers

Milan Radovich, Chief Precision Medicine Officer, Caris Life Sciences

biopharma companies can develop new medicines and diagnostics in the future, as science, treatment landscapes, and patients’ unmet needs evolve.

“All increases in longevity have resulted from scientific or technological breakthroughs. The advent of microscopes, for example, directly led to the discovery of bacteria and the development of antibiotics. Next-generation sequencing is the new microscope. It has revealed new strategies, not just in oncology, but across all therapeutic areas,” said Spetzler. “New precision therapeutics are being launched, with almost one new indication approved every week. This is just the beginning, and we are confident that there is so much more to come.”

Building partnerships throughout the lifecycle

Caris partners with biopharma at all stages, from target identification that informs the development of novel medicines, through clinical development to accelerate the process, to the commercialization of new precision-medicine drugs that can transform

patient care. The company's commercial profiling capabilities fuel its real-world data solutions and new drug and target discovery.

For Caris' biopharma profiling partners, WES and WTS data on clinical trial populations increase researchers' ability to interrogate and understand underlying disease biology, and to find molecular drivers and biomarkers of response and resistance. Getting the most out of every sample reduces the risk of researchers missing potential signals and future-proofs the dataset. This ultimately increases the probability of success for a differentiated novel therapy in a crowded treatment landscape.

Caris' biopharma partnerships go beyond research and development (R&D); the company partners with biopharma to leverage data to optimize commercialization strategies, as well as to support payer-reimbursement discussions at launch.

"One of the benefits of Caris' approach is the use of the same testing backbone in real-world patient populations and in clinical trial cohorts. This can help drug developers understand, optimize, and extrapolate the potential of their drugs early in their development process. The approach provides partners with confidence in analysis and decision making from target discovery and drug development to registration. It also supports the development of a companion diagnostic for subsequent commercialization," said Spetzler.

As of February 2023, Caris' real-world database has over 455,000 genomic profiles, with 350,000 matched clinical profiles. The wealth of data, together with whole-slide imaging and artificial intelligence (AI) integration, can help biopharma partners gain insights about outcomes for specific biomarker cohorts and tumor microenvironments, to aid the selection of ideal populations for clinical trials.

"The paradigm by which companies are developing novel medicines is changing. The most impactful medicines of the future will have leveraged data at an unprecedented scale and infused precision medicine from the earliest stages of drug development," said Brian Lamon, Caris' CBO and head of biopharma business development. "That being said, not all data is equal. Our real-world dataset is more heterogenous than other available datasets, with a majority of profiles coming from patients treated in the community setting. Caris' broad geographic distribution of testing centers—in rural and urban areas with a high percentage of minority and underserved populations—means that our patient population is truly representative of the overall patient population."

Identifying the best targets for drug development

By combining its industry-leading clinico-genomic database and tissue repository, Caris' Discovery platform enables biopharma partners to identify novel and clinically relevant targets, agnostic of modalities. The ability to use real-world WES and WTS data and patient tissues to identify and validate targets provides biopharma partners with access to actionable, cancer-specific targets, along with the ability to rapidly screen out targets that are inactive or that have unacceptable toxicity profiles.

"Caris' database is a treasure trove for biopharma seeking to discover new cancer vulnerabilities, drug targets, and predictive biomarkers," said Radovich.

In addition to its comprehensive datasets, Caris has developed a strong infrastructure to deliver on this

Novel circulating nucleic-acid sequencing

WES + WTS solution	Variants and signatures Data for whole exome and transcriptome and informed signatures (MSI, bTMB, gLOH)
Buffy coat normal correction	Reduce false positives Assessment of CHIP mutations; improved bTMB calculation; incidental germline analysis
cfDNA and cfRNA input	Reduce false negatives More material increases detection rate in low-shedding tumor types

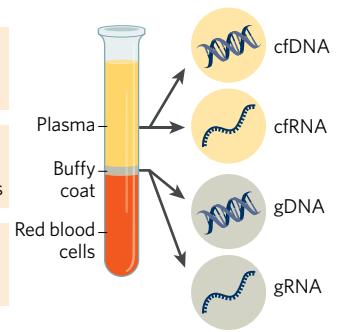


Fig. 2 | Caris' liquid-biopsy platform, Caris Assure, provides a comprehensive and non-invasive approach to profiling. bTMB, blood tumor mutational burden; cfDNA, cell-free DNA; cfRNA, cell-free RNA; CHIP, clonal hematopoiesis of indeterminate potential; gDNA, genomic DNA; gLOH, genome-wide loss of heterozygosity; gRNA, genomic RNA; MSI, microsatellite instability; WES, whole-exome DNA sequencing; WTS, whole-transcriptome RNA sequencing.

promise, with 60,000 square feet of discovery lab space. The company has dedicated scientists who can validate and characterize potential discovery targets through a variety of platforms, including protein expression, antibody sensitivity and specificity, cell-surface expression, and epitope mapping.

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Brian Lamon, CBO & Head of Biopharma Business Development, Caris Life Sciences

Maximizing data from every sample

The recent addition of the Caris Assure liquid biopsy (Fig. 2) means the company can offer patients and biopharma partners access to a non-invasive liquid-profiling option. It also means that its database of patient molecular profiles will be further enriched with the data from this unique assay. Staying true to Caris' core belief of maximizing data from every patient sample, Caris Assure employs a consistent WES and WTS approach for blood samples and analyzes cell-free DNA and RNA from plasma as well as genomic DNA and RNA from white blood cells.

Caris Assure will bring clinical utility for therapy selection, treatment monitoring, and detection of minimal residual disease. It will also enable patient-friendly options for longitudinal molecular profiling over time, increasing the ability of Caris and its partners to tackle elusive questions around response and resistance, and to identify biomarker-based approaches that realize the potential of precision medicine.

Tailoring partnerships to accelerate the next wave of therapeutics

Caris focuses on creating broad-based and flexible partnerships in order to maximize value for its partners. By creating partnerships that include

access to both real-world data and clinical trial profiling on the same technology backbone, Caris unlocks the synergies of the two individual solutions and potentiates the value of each alone for both its biopharma partners and future patients.

"At the end of the day, broader partnerships with Caris' profiling platform enable innovative biomarker exploration. A more detailed understanding of biomarkers allows companies to design stronger clinical trials, and reliable data give companies more confidence in investment decisions made around a particular drug or program," said Lamon.

Caris can tailor agreements to individual companies and programs centered around partners' individual needs. This flexibility is supported by a purpose-built biopharma business-development team that includes passionate and experienced people with years of in-depth drug development and diagnostic experience. The dedicated biopharma molecular science partnering team exemplifies the company's approach to investing in people and building in-house groups.

"The carefully recruited individuals in our molecular science team partner with biopharma business-development leads to ensure that biopharma partners can access the right solutions and make the most of available data. This team helps our biopharma partners understand the data and get the most out of the partnership," said Lamon.

Building the future on big data

Caris' goal is to find the best drug for every patient. To reach this aim, the company is committed to evolving its technologies and data platform to meet the needs of biopharma, physicians, and patients into the future.

"We aim to infuse precision medicine throughout the R&D process, in order to create better clinical trials and to allow unsuccessful drug candidates to fail faster so that research can push forward. In order to achieve this, we want to grow our biopharma partnerships. We are working to ensure that patients can hear 'we have a personalized treatment that can help your type of disease' more often in the future," said Lamon.

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